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Contents.

CONTENTS—Continued
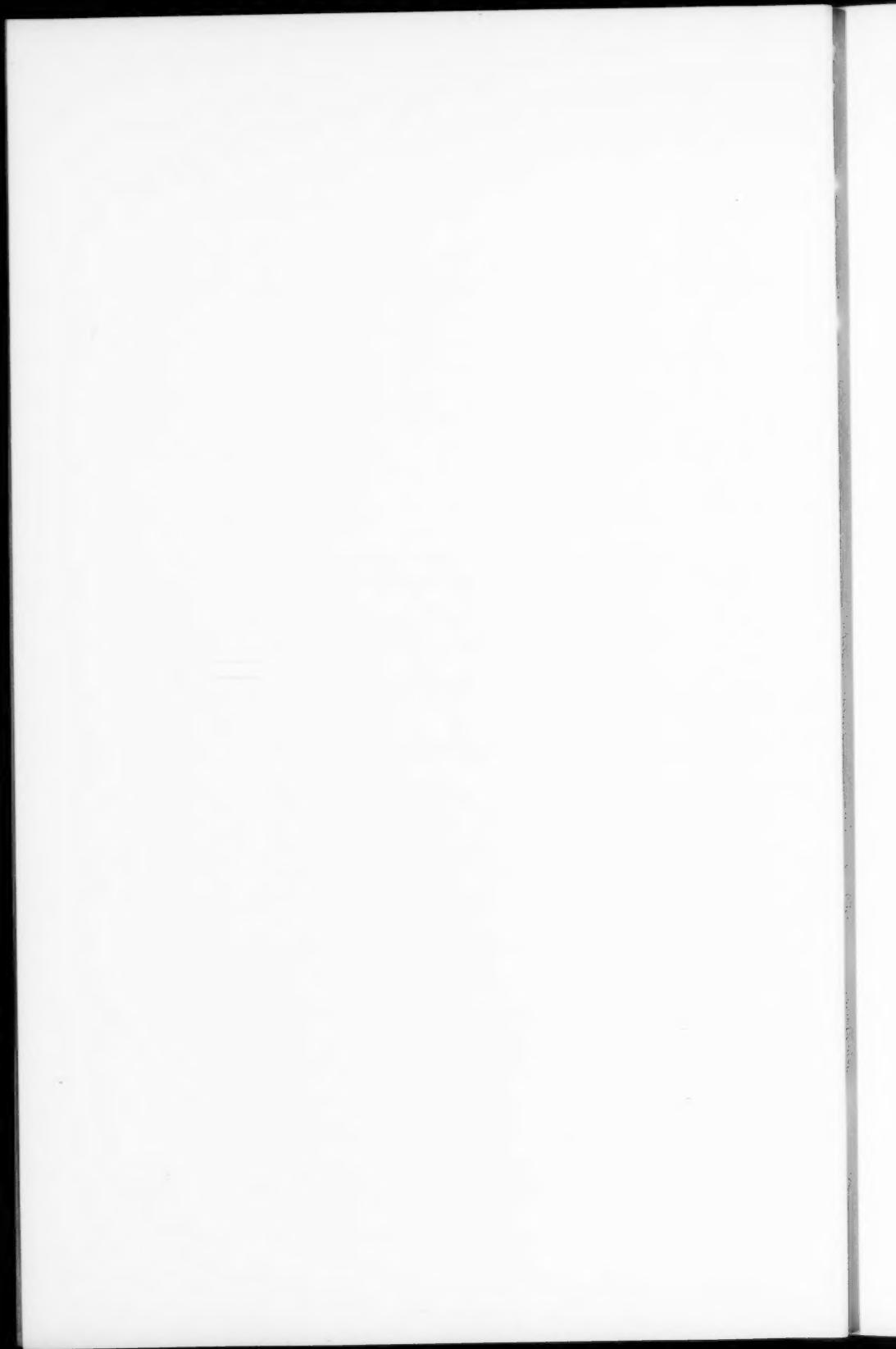
I

THE PROTECTIVE MECHANISMS
OF THE BAT'S EAR

ERNEST GLEN WEVER

AND

JACK A. VERNON

PRINCETON, N. J.

In all the higher vertebrates the ear is provided with means for its protection against sounds of extreme intensities. This protection is required for the sensory structures of the cochlea, and especially for its hair cells, for these are the cells that show the first evidences of damage when the ear is overstimulated.

In most animals the protection is afforded by the muscles of the middle ear, whose contractions add friction and tension to the ossicular motions and thereby reduce sound transmission.

It has been suggested that the bat's ear has a particular need for this protection, at least in the common species that capture insects by echolocation, for this performance requires the production of repeated cries of great intensity, often continued over long periods of time. In some circumstances, as when flying about in caves, the ear will also be exposed to the clamor of other bats.

We have recorded cries in *Myotis lucifugus* with root-mean-square sound pressures of 60 dynes per sq cm, and Griffin[1] has observed

pressures of this same order and possibly higher. These measurements were made at distances of 5 to 10 cm from the bat's mouth, and the pressures would of course be greater in the immediate vicinity. Even though, as some have supposed, the sound is emitted in a concentrated beam and takes a forward direction, the ears must receive a heavy stimulation, and this will occur many thousands of times during an evening of insect hunting. Without some form of protection, these sounds would be expected to produce a temporary impairment of sensitivity, even though they might not cause permanent damage. Hartridge[2] has suggested further that the bat's ear needs to be protected precisely during the emission of a pulse and then must at once be returned to its full sensitivity in order to receive the echo from the object being explored.

Like all the other mammals, bats are provided with a pair of tympanic muscles, the tensor tympani and stapedius muscles. In addition we have identified two other protective mechanisms, a folding of the auricle so as to shield the entrance to the meatus, and a closure of the meatus itself. All three of these mechanisms are operated reflexly on stimulation of the ear with loud sounds, though they do not necessarily respond under the same conditions.

<div align="center">PROCEDURE</div>

These mechanisms have been studied in the little brown bat, *Myotis l. lucifugus*, by use of the cochlear potentials. In the standard procedure, the animals were anesthetized with Pernoston, the round window of the right ear was exposed by a lateral approach, and an electrode was placed on the round window membrane. The ear was stimulated with tones from one of a pair of loudspeakers that together covered the range of frequencies from 100 to 100,000~, and the cochlear potentials were recorded with two selective voltmeters (wave analyzers) that operated over this same range. The loudspeakers were connected to a sound tube that led through the wall of a soundproof, shielded room to the animal's ear. Sometimes the experiments required two separate stimulating systems, one for each ear, as described below. The sound pressures at the animal's ear were measured with a microphone calibrated over the complete range of frequencies. Further details of the procedure and methods of calibration are given in an earlier article.[3]

<div align="center">RESULTS</div>

1. *The Auricular Folding Mechanism.* A bat held in the hand, or resting quietly on some surface, will often respond to a strong
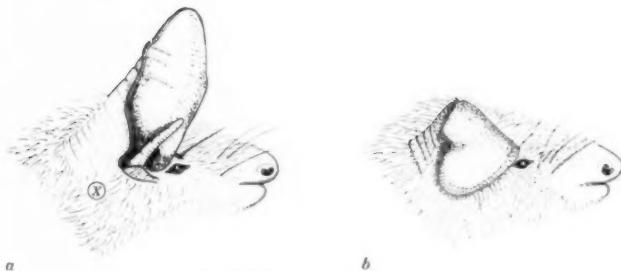
Fig. 1 a.—Head of Myotis lucifugus seen from the right side, with the auricle in the erect position. The tragus is seen rising from the depths of the auricular opening. X marks the location of the meatal valve, shown in Figure 3. b. The same view, with the auricle folded in response to a sound.

sound, as of a Galton whistle operated at its highest frequency, with a momentary bending of the tip half of the auricle. The bending occurs along a prominent crease and takes a form shown in Figure 1 b. It is easy to imitate this folding in an anesthetized animal, or even in a preserved specimen, for on the application of force in the proper direction the outer portion of the auricle takes a folded position in a rather uniform way. Other forms of movement of the auricle occur also, and another common one is a sharp backward bending of the whole structure, but the one illustrated here gives the greatest protection to the ear.

We have made use of the cochlear potentials to obtain an indication of the effectiveness of this auricular folding in reducing the passage of sounds into the ear. The potentials were first measured for numerous tones with the head at a standard distance of 10 cm from the end of a sound tube, with the animal facing the tube and the auricles erect. The auricle of the right ear was then folded over and held in a position that imitated as closely as we could judge the folding that the animal itself is able to produce, and the measurements were repeated. The differences between the two sets of measurements represent the effects of the folding, and are given in Figure 2. The changes are shown on the ordinate as decibels of attenuation.

As may be seen, the effect for the low tones was a moderate improvement of response, but beyond 1000~ there was a decrease varying between 9 and 17 db, and then at 10,000~ and beyond the decrease was of the order of 20 db. The folded auricle did not by
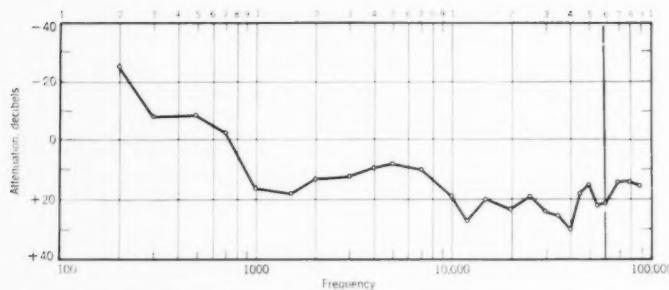
Fig. 2.—Effects of auricular folding on the transmission of sounds into the ear, shown relative to the normal condition with auricle erect (zero line).
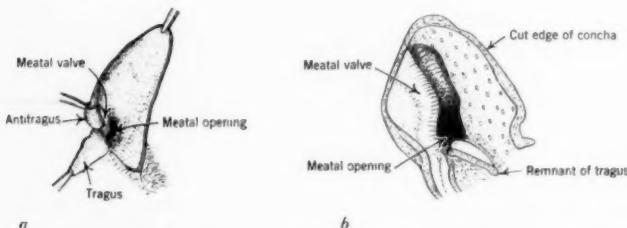
Fig. 3 *a.*—The auricle pulled open and the tragus bent down and back to show the meatal valve and meatal opening. The view is more from the front than that of Figure 1. *b.* The deep portion of the concha, showing the meatal valve and opening after cutting away most of the auricle and tragus. The orientation is the same as in *a.*

any means provide a tight covering of the ear's orifice, yet its barrier effect was substantial, especially for the high frequencies.

2. *Closure of the Meatus.* Deep in the external auditory meatus, within about 2 mm of the drum membrane, is a semilunar protuberance on the lateral wall. It is formed by an inward fold of the auricular cartilage, but its presence is not evident to view from the outside because the crevice has become filled in with fat and connective tissue over which the skin of the auricle is smoothly stretched. This structure, shown in Figure 3, serves as a valve in the meatal opening.

When a well awakened and lively bat was held in the hands for a long time, until it grew somewhat accustomed to the restraint, it was possible to adjust its position under a binocular microscope so
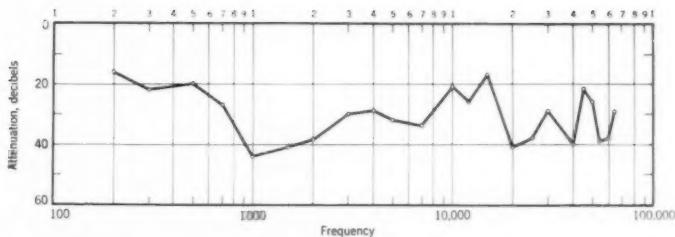
Fig. 4.—Effects upon sound transmission of action of the meatal valve.
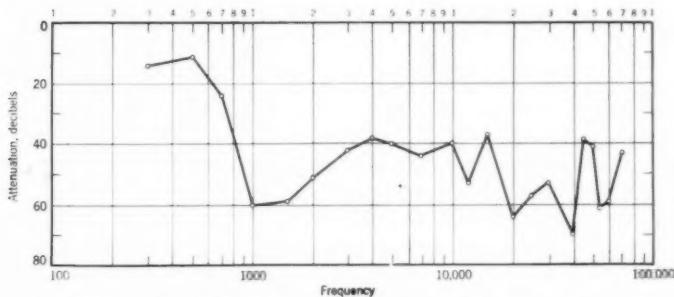
Fig. 5.—Combined effects of auricular folding and closure of the meatus.

that the deep cavity of the meatus could be seen. We used a microscope with 10 times magnification and directed a strong light into the cavity. When the auricle was placed at the proper angle the meatal valve could be brought into view, and if then an intense tone were sounded its action became clearly evident. In response to the sound the protuberance moved medially so as to form a tight closure of the meatal opening.

We have imitated the closure in the anesthetized animal by pushing on the cartilaginous fold from the outside at a point indicated by X in Figure 1 a. By recording the cochlear potentials before and after this closure we have obtained a measure of its effects upon sound transmission. Some of the results are given in Figure 4. As may be seen, the attenuation varies between 20 and 40 db over the frequency range.
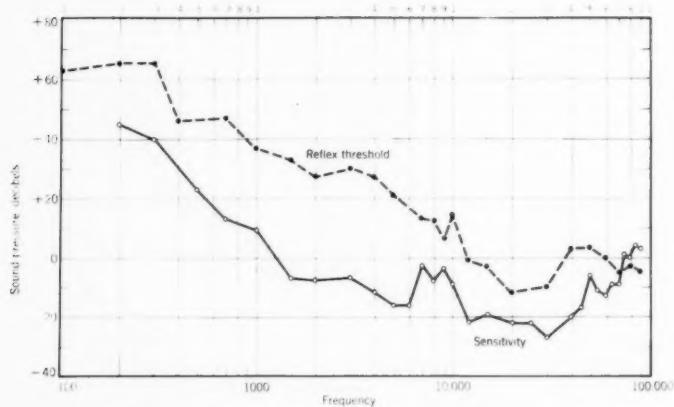
Fig. 6.—Reflex thresholds for the tympanic muscles, for various stimulating tones(dashed line), and a sensitivity curve for the stimulated ear (solid line). The sound pressure is represented in decibels relative to 1 dyne per sq. cm.

When the auricular folding and meatus closing are combined, the results are as shown in Figure 5. Here the protective effects are substantial, varying mainly between 40 and 60 db for tones above 1000~, and even attaining 70 db at 40,000~.

We have not yet worked out all details of the action by which these forms of protection are achieved.

3. *The Tympanic Muscles.* For a study of the actions of the muscles of the middle ear and their effects upon sound transmission, the bat was first lightly anesthetized with ether and then decerebrated, after which a period of time was allowed for the elimination of the anesthetic and recovery from the shock of the operation.

The auricle of the right ear was sealed into one sound tube, and another sound tube, leading from a separate loudspeaker, was fitted to the left ear. This arrangement served for several series of observations, now to be described.

a. The Tympanic Reflex Threshold. The right ear was stimulated with 3000~ at the sound pressure necessary to produce a response

Attenuation, decibels

0

10

20

30

Perfect regulation

−30 −20 −10 0 +10 +20 +30

Level of eliciting tone, db
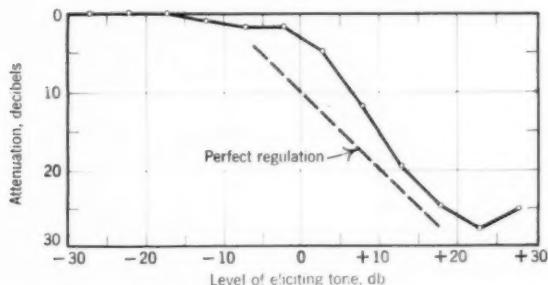
Fig. 7.—Increased effectiveness of the tympanic muscle reflex in reducing transmission as the level of the acoustic stimulation is increased. This level is shown on the abscissa in decibels relative to 1 dyne per sq. cm. The broken line indicates the slope of the function for perfect regulation: an increase in attenuation that equals the increase in the level of stimulation.

of 3 microvolts, and this stimulation was steadily maintained. The left ear was then stimulated briefly with various tones, which were first presented at low levels and then were increased by small steps (usually 1 db) until a clear diminution of the response in the right ear indicated that the reflex threshold had been crossed. This procedure rests upon the fact that the tympanic reflex is bilateral: an effective stimulation of the left ear produces a contraction of the muscles in both ears.

The results of this procedure for a representative animal are shown by the broken curve of Figure 6. Large sound pressures are required to elicit the reflex in the low frequencies, and then as the frequency is raised the threshold falls until it reaches its lowest point around 20,000~. Shown in the same figure is a sensitivity function for the left ear, which represents the sound pressure necessary to produce a response of 1 microvolt. It is evident that the two curves have somewhat the same form, though they approach one another more closely in the upper frequencies. For the middle tones, from 700 to 6000~, the reflex threshold is reached at levels 30 to 40 db above those necessary to produce 1 microvolt, whereas in the range beyond, up to 60,000~, this difference is only about 10 db. At still higher frequencies the reflex is elicited by sounds that are still too weak to produce our arbitrary standard. Hence it appears that the reflex threshold bears a general relation to sensitivity as measured by the cochlear potentials, but that a further factor operates to enhance the effectiveness of the higher tones.
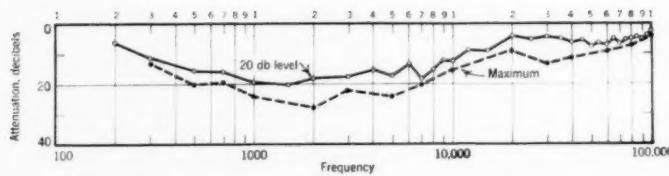
Fig. 8.—Frequency relations for the tympanic muscle reflex. The atten-
uation was measured for various tones in the right ear when the left ear was
briefly stimulated with a 10,000~ tone to elicit the reflex. For the solid
curve the 10,000~ tone was presented at a level 20 db above the reflex
threshold, and for the broken curve it was presented at a level giving the
maximum attenuation.

b. Intensity Relations. In a second series of experiments the
stimulation in the right ear was continued at a constant level as before,
and the stimulation in the left ear was raised to various levels beyond
the reflex threshold. This procedure was carried out for a number of
tones in the left ear, and for all of these the potential recorded in the
right ear became progressively smaller as the contraction of the muscles
was made more vigorous, until at a high level a maximum was reached.
Figure 7 shows a curve for which the eliciting tone in the left ear was
40,000~, and the tone in the right ear (the ear in which the measure-
ments were made) was 3000~.

The dashed curve of this figure is drawn to represent the slope
that would obtain if the increase in the sound pressure of the stimu-
lating tone was exactly counteracted by an increased action of the
middle ear muscles. The experimental curve indeed approximates
this form in its middle region, though departing from it at the ends.
Beyond a level of about 10 db above the reflex threshold, the effective
stimulation of the ear is maintained at nearly a constant value, until
a point is reached at which this regulation fails. Here the point of
failure lies about 40 db above the reflex threshold, and this point no
doubt represents the maximum contractions of which the tympanic
muscles are capable.

c. Frequency Relations. In a further series of experiments the
right ear was stimulated with various tones, each maintained at the
sound pressure necessary to produce a response of 3 microvolts, and
the left ear was stimulated briefly with a tone of 10,000~ at levels
well above the reflex threshold. The effects of the muscle action were

then observed as reductions of the potential recorded from the right
ear.

Some of the results are given in Figure 8.   For the solid curve
of this figure the 10,000⌐ tone in the left ear was presented at a
level 20 db above the reflex threshold for this tone.   For the dashed
curve this tone was presented at the level required to produce a maxi-
mum attenuation of the tone under observation in the right ear.   The
two curves take much the same course.   They show that the tympanic
muscles provide the greatest protection for tones in the range from
700 to 8000⌐, for which this protection reaches a maximum of 20 to
27 db.   For the higher tones the protection is less, amounting to no
more than 13 db for 30,000⌐ and declining to 4 db for 100,000⌐.
The 20 db curve is probably better representative of practical amounts
of protection, as the maximum contractions of the muscles can hardly
be sustained for any length of time.   At this level only 4 to 7 db of
protection is afforded for the important range of 20,000 to 70,000⌐,
which is the range of the bat's vocal pulses in echolocation.   The bat's
middle ear muscles are effective in protecting against tones of inter-
mediate and moderately high frequency, but are of little service in
protecting against those of very high frequency.

COMMENT

Mention has already been made of Hartridge's suggestion that
the bat's ear needs to be protected against his own outgoing pulse if
he is to hear the faint echo when it arrives.   Hartridge believed that
a properly timed contraction of the middle ear muscles would provide
this protection.   These ideas have met with wide acceptance, though
no evidence has been presented apart from the analogies of radar and
sonar, in which the receiving circuit is switched off at the moment of
transmission of a signal.

The Hartridge hypothesis raises two serious questions, both of
which were discussed by Griffin.   The first question is whether the
tympanic muscles are able to relax in the brief times available between
the production of a pulse and the return of its echo.   Griffin regarded
this as a possibility, though not a very likely one.

The second question is whether the middle ear muscles of the bat
can provide protection against the high tones.   The evidence obtained
from studies of the action of these muscles in other animals is not
altogether encouraging in this regard.   Wiggers[4] observed the changes
in the transmission of various frequencies caused by spontaneous con-

tractions of the middle ear muscles in guinea pigs, and found reductions around 40 db for 100⁓ and progressively smaller reductions as the frequency was raised to 1000⁓. There were then slight improvements between 1300 and 1800⁓, and no significant changes from 1800 up to 2500⁓ where the observations ended. Studies of our own[5] on the effects of acoustically aroused contractions in cats likewise showed the greatest effects for the low tones, slight improvements in a narrow region from 600 to 800⁓, and then only moderate reductions for higher frequencies.

In defense of Hartridge's position it is usually argued that in the bat's ear the whole action pattern of the muscles has been shifted upward in frequency so as to include within the operating range the sounds used in echolocation. Griffin examined the evidence on this question and concluded in favor of the argument as stated, largely on a basis of some observations of Galambos.[6]

In his study of the cochlear potentials in the bat, Galambos reported a transient rise when a strong tone was suddenly presented to the ear, and also when the ear was under steady stimulation and the animal was killed by injecting a poison into the blood stream. The rise was interpreted as representing a brief period during which the sound was operating without any restraining action of the middle ear muscles, in the first situation because of the latency of the acoustic reflex and in the second situation because the poison acts on the neuro-muscular system before it acts on the cochlea.

In further support of Hartridge's position it is often said that the bat's middle ear muscles are very large relative to the other parts of the ear. The pertinent consideration here is the tension that the muscles can exert in relation to the mass of the vibrating structures.

To gain a preliminary idea of this relation in the bat's ear we have made a few measurements of the form and size of the tympanic muscles and the mass of the ossicular mechanism. Also, for purposes of comparison, we have made similar measurements on these structures in cats.

For the bat (*Myotis lucifugus*) the tensor tympani muscle is spindle-shaped, and in the cat it varies between this form and a distorted cone. A study of these muscles in cross section reveals a striking difference in internal structure. The cat's tensor tympani muscle contains a large central core of tendon fibers, making up about half of the total bulk. In the bat the tendon anchoring the muscle to the

TABLE I

ANIMAL	T TENSOR MUSCLE, MG	S STAPEDIUS MUSCLE, MG	O OSSICLES AND DRUM MG	RATIO T/O	RATIO S/O
Bat 1	0.142	0.188	0.170	0.82	1.10
Bat 2	0.111	0.111	0.100	1.11	1.11
Cat 1	5.81	1.67	12.4	0.47	0.14
Cat 2	5.31	1.25	13.2	0.50	0.10

malleus is prolonged somewhat along the surface adjacent to the cochlea, but the tendinous material comprises only about 16 per cent of the total.

The stapedius muscle in the bat is conical, whereas in the cat it is fan-shaped. In both the tendinous content is but 4 to 6 per cent of the total.

In our measurements, most of which were based upon graphic reconstructions from serial sections, we have determined the actual muscle fiber content of these structures. Some of the results are given in Table I. For one of the bat ears the tensor tympani muscle had a muscle mass of 0.142 milligrams, and the stapedius muscle a mass of 0.188 mg. In this ear the three ossicles together with the drum membrane weighed 0.170 mg. Accordingly, the ratio of masses of the tensor muscle to the ossicular mechanism was 0.82, and this ratio for the stapedius muscle was 1.10. The masses for all three structures were smaller for the second bat, but the ratios were similar. For one of the cats the muscle fiber content of the tensor tympani muscle was 5.81 mg, and this value for the stapedius muscle was 1.67 mg. The ossicles and drum membrane of this ear weighed 12.4 mg. Hence the ratio of tensor tympani mass to ossicular mass was 0.47, and the ratio for the stapedius muscle was 0.14. The second cat showed similar relations.

These observations show that the tensor tympani muscle in the cat has about half the mass of the moving structures, and the stapedius muscle has about one-seventh of this mass. For the bat each of the muscles has about the same mass as the ossicular structures. The results therefore are in support of the contention that the bat's middle ear muscles are large in relation to the function that they serve, at

least in comparison with the cat.   The relative magnitude of the bat's
stapedius muscle is particularly striking.

No direct measurements have been made of the maximum ten-
sions exerted by these muscles in the bat.   Some data are available for
cats.   An earlier study by the use of a strain gauge gave mean values
of 4.4 grams or 4300 dynes for the cat's tensor tympani muscle and
1.6 grams or 1570 dynes for the stapedius muscle.[7]   We know also
that in the cat the stapedius muscle is the more effective in reducing
sound transmission despite its smaller size.[8]   If the same relation holds
for the bat, then the comparatively large size of the stapedius muscle
gains in impressiveness.

From these observations we might expect an unusually great
attenuation of sounds by the bat's tympanic muscles, but in fact the
attenuation is of the same order of magnitude as in the guinea pig and
cat.   It extends, however, into a higher range of frequencies.   The
higher range of control of transmission in the bat's ear is a function of
the smaller masses of the vibrating structures and—if we can argue
from the relative size—a relatively greater muscle action, especially
for the stapedius muscle.

In both bat and cat the tympanic muscles serve effectively in
protecting the ear against the lower tones of the animal's working
range, but give little protection against the upper frequencies.   In
the bat this protection is supplemented by the ear-closing mechan-
isms, which are particularly advantageous in the upper range.

The different ranges of operation of the two types of mechan-
isms are reasonable on theoretical grounds.   The tympanic muscles act
by the exertion of tension, and the tension has two effects.   The ten-
sion as such reduces transmission for the low tones by adding stiffness
to the vibratory system, but as the frequency rises this effect falls off
progressively and may even turn into an enhancement for certain
tones, as is seen in the cat.   Because the muscles are carried along in
the vibrations of the ossicles their contractions add friction also,
and actually it seems that the frictional effect outweighs the other
over most of the frequency scale.   In the uppermost frequencies this
muscular friction is ineffective because it becomes small relative to
the inherent friction of the vibratory system—friction in the drum
membrane, ligaments, joint surfaces, cochlear fluid, and in the air
layers bounding these parts.

A barrier, as we know from architectural acoustics, exhibits an
entirely different relation to frequency.   It is not very effective in

blocking the transmission of low-frequency sounds, but becomes increasingly effective as the frequency is raised. The bat, with its development of sensitivity in the upper frequencies, beyond the range of adequate action for a tympanic muscle system, has acquired the two types of barrier mechanism described here.

The form of action of the tympanic muscles in the bat may well be advantageous in the presence of powerful low-frequency noise. A contraction of these muscles can protect against such noise without causing much impairment of the bat's ability to hear his echo-ranging signals. By having three different protective mechanisms at his command the bat is remarkably well equipped to cope with the many complex and changing characteristics of his auditory world.

110 ENO HALL

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II

SOME HIGHLIGHTS OF SCIENCE
IN OTOLOGY

Hallowell Davis, M.D.

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We hear repeatedly of the contributions to the understanding, the cure and the prevention of disease that flow from the study of the basic sciences; but in our enthusiasm for the basic sciences and in our present very legitimate concern to promote interest and, above all, education in the basic sciences it is just as well to remember that the flow of knowledge and the inspiration by new ideas is a two-way affair, and that the practitioners of the art of medicine and those who engage in clinical research have directly or indirectly made many contributions to our basic understanding of the workings of the human mind and body.

All aglow with these sparkling generalities, I have examined the situation in the case of deafness and the understanding of hearing.

It is my personal impression, however, that the exchange of ideas between physics, physiology, and psychology on the one hand and the clinical study of hearing on the other has been less free and stimulating than has been the corresponding interchange in many other areas of medicine and medical science. Only with anatomy has otology kept a really close liaison. This is worth a few moments' consideration.

In the first place otology is, of course, a branch of surgery. Infections and neoplasms of the ear, nose, and throat are serious threats to life. Loss of hearing, on the other hand, although it may be extremely inconvenient, is not fatal. The primary concern of the otologist has always been to care for the life of the patient with his special surgical skills, and he has on the whole been more interested in hearing loss and the symptoms of tinnitus and of vertigo as diagnostic signs to guide him to the source of infection, and so forth, than as handicaps

to be overcome by his surgical skill. On the other hand the surgery of the ear, nose, and throat involves probably the most complex anatomy of the human body and, with the rise of pathology as a medical science, the otologist has studied with care the anatomy and the pathology, both gross and microscopic, of the organs in his area of interest.

The study of the finer microscopic details of the inner ear, particularly in the human, has been seriously handicapped by the inaccessible anatomical location of the cochlea within the temporal bone. The bone prevents ready access of fixatives to the tissues unless they are injected, as in animal experiments, by way of the circulatory system (after washing out the blood) at the moment of death. Even with animals, the necessity for decalcifying the bone before sectioning it for the microscope has been a serious handicap to careful anatomical study. As a result, the flow of knowledge has been almost completely from the professional anatomist toward the pathologist and surgeon rather than in the reverse direction, even though the mutual interchange has been much better in this area than in physics or physiology or psychology.

Hearing is a psychological, subjective function and is very difficult to study under clinical conditions. Only recently have the methods of psychophysics, with their elaborate controls of experimental design, avoidance of unintentional cues to the subjects, appropriate selection of subjects, control of motivation, and statistical analysis of the data been applied to the study of hearing. Really good psychophysical techniques are almost impossible under clinical conditions. Not all patients have the time, the intelligence, or the motivation to become good subjects for psychophysical experiments.

Because the endpoint of hearing is subjective, and therefore requires the special techniques of psychoacoustics to bring it within the realm of exact science, hearing became a province of psychology. The attention of physiology was turned to circulation and respiration, to excretion, to metabolism, to endocrines, to homeostasis, to muscle and nerve. Not until the development of modern electronics and electroacoustics provided new tools for the control of the acoustic stimulus and for the measurement of small electrical signals, of small movements of vibrating parts by stroboscopic observations under high-powered microscopes, and so forth, did physiologists and biophysicists begin to take a serious interest in the normal functions of the ear.

Meanwhile, otology was concerned with infection and neoplasm, with antibiotics, and with allergy. Only recently, with the advent

of the fenestration operation, has the improvement of hearing become
a major and direct objective of surgery. The fenestration operation
has contributed very considerably to human happiness and so also has
the stapes mobilization operation for those patients who are fortunate
enough to "get a good break." They have not, however, contributed
to basic knowledge except to confirm concepts that had already been
well established in biophysics.

Let us now examine a few specific instances where the study of
deafness and hearing loss has indeed advanced our fundamental knowl-
edge.

In the area of embryology and developmental anatomy a major
study by Drs. Barry Anson and T. H. Bast was initiated by a desire
to determine, if possible, the nature and cause of otosclerosis. Oto-
sclerosis depends on the growth of an abnormal type of bone, usually
arising from a particular part of the otic capsule. When the new
bone involves the footplate of the stapes it fixes the latter firmly in
the oval window and interferes seriously with the transmission of
sound to the inner ear. The new bone has several characteristics of
embryonic bone, and it was plausible to suppose that it might arise
from remnants of such tissue.

Drs. Anson and Bast have traced in detail the very complicated
story of the embryological development of the inner and middle ear
and the adjacent structures, including the fissula ante fenestrum,
where the otosclerotic foci most often arise. This information is now
the definitive description of the development of the human ear from
its embryological origins. The specific hypothesis concerning otoscler-
osis that initiated it is not proven nor is it completely disproven,
although it now seems to be no more than a contributing factor at
most.

Drs. Anson and Bast are anatomists and they have worked as basic
scientists. They were directly inspired, however, by a clinical prob-
lem: the problem of the exact nature and cause of otosclerosis. It is
worth mentioning also that they have been materially assisted over the
years by financial support from the Central Bureau of Research of the
American Otological Society. This is another form of a contribution
from the study and treatment of disease to fundamental science. And
I may add that similar generous support to other laboratories such as
that of Professor Elmer Culler, and also our own at Harvard, during
critical years of the depression and World War II, was of invaluable
assistance to fundamental psychological and physiological studies.

The individual otologist who, through his stimulation of others and by his own observations, has contributed the most to fundamental knowledge of hearing during the last thirty years is, in my opinion, Dr. Edmund P. Fowler, Sr.   Dr. Fowler has been, and at 86 years of age still is, a practicing otologist in New York City.   To him we owe the impetus for the development of the electric audiometer and also the discovery, with this instrument, of the phenomenon in hearing that he has named "recruitment of loudness," to which I shall return later.   But Dr. Fowler's discovery of recruitment depended on the development of a new instrument, the electric audiometer.

The development and construction of the first commercially produced electric audiometer was actually carried out at the Bell Telephone Laboratories under the leadership of Dr. Harvey Fletcher.   The resulting Western Electric 2A audiometer was the first commercial audiometer to employ vacuum tubes and the first electric audiometer to come into wide use in laboratories and in clinics.   The quantitative measurement of human hearing in terms not only of frequency in cycles per second but also in terms of intensity in decibels of sound pressure level is the foundation of modern psychoacoustics.   Dr. Fowler played a part in initiating this development.   Here is the story of the origin of the Western Electric audiometers, as told to me by Dr. Fowler in correspondence and personal interview.

In 1919, after his return from military service in World War I, Dr. Fowler found himself with a very small otological practice and consequently plenty of time on his hands.   More than most otologists of his day, he was interested in hearing as well as in diseases of the ear. He was not satisfied with tuning forks as instruments with which to measure hearing.   They were accurate in frequency but, unless used in a very time-consuming way, yielded only very rough estimates of the sensitivity of hearing.   It happened, and here is one of those lucky accidents in the history of science, that a near neighbor and a good friend of his in Spuyten Duyvil-on-the-Hudson, Mr. Alexander Nicolson, was a physicist-engineer and happened to be engaged in growing large Rochelle salt crystals and studying their piezo-electric properties.   These crystals and their ability to transform electrical potential differences into mechanical movement and vice versa (the piezo-electric effect) have since become the basis of an important class of electroacoustic transducers used in microphones, in the receivers of hearing aids, in phonograph pick-ups, in hydrophones, and elsewhere. Dr. Fowler conceived the idea of recording test signals on a phonograph disk, playing them back through crystal pick-ups and headphones and using them to measure quantitatively the sensitivity of

human hearing. Remember that the thermionic valve or vacuum tube was then still quite new. It had been used in communication and signal systems during World War I but was only just at that time being used in physiological research for the first time by Dr. Alexander Forbes, in Boston.

Dr. Nicolson and Dr. Fowler constructed an apparatus, using the phonograph disk and Rochelle salt crystals. "It was pretty crude," writes Dr. Fowler, "but it worked. We took it to Dr. Harvey Fletcher, who said, 'We can do better than this using the thermionic valve.' He asked me to co-operate, which, of course, I was only too anxious to do. Harvey was the head of the acoustic research laboratory of the Western Electric Company. You know the wonderful group he had around him."

At this point, let me say that I certainly do know Dr. Harvey Fletcher and "the wonderful group he had around him." If Dr. Fowler was the outstanding figure in scientific otology in America in the first half of the twentieth century, the corresponding figure in psychoacoustics was Dr. Harvey Fletcher, the first president of the Acoustical Society of America.

Here let me quote, from a letter, Dr. Fletcher's terse statement of why the Bell Telephone Laboratory became interested in making audiometers. Dr. Fletcher writes: "Some friends of our executives were hard of hearing and were sent to us as engineers to find out the degree of hearing loss and to see if we could do anything to correct their hearing deficiency. That started the development of audiometers." He also remarks: "It is my opinion that we would have now about the same instruments that we had previously to 1925 if the vacuum tube had not appeared."

Dr. Fletcher is probably quite right, although the electric audiometer constructed by Bunch and Dean in 1919 was a valiant attempt to do the job with a motor-generator and tachometer instead of Fletcher's vacuum tube oscillator. It might or might not have been improved sufficiently to displace the set of tuning forks as the primary instrument of audiometry.

But let me get back to Dr. Fowler's reminiscences about the first electric audiometer. He continues:

"In a sound-proofed room, about eight feet square, Harvey Fletcher mounted his various electronic devices so that the floor and

all four walls were practically covered with wires and gadgets, all of which subsequently were concentrated into a phonograph console cabinet and constituted the 1A audiometer, which still sits in my soundproofed room at 140 East 54th Street. I sent down to Western Electric many of my patients so that we could obtain audiograms of various types of ear disorders affecting the hearing, and gain experience in the techniques of testing and in setting up an average normal threshold. Mr. R. L. Wegel was assigned to collaborate with me in constructing an audiogram chart and the proper frequency and intensity scale which would be of the most use to the otologists.   Since all sensations are sensed logarithmically, and the usual musical scale is a logarithmic scale, I thought that we should retain the octave frequency scale familiar to the otologist.   "Decibel" was then an unknown word to them. After much discussion, an audiogram chart evolved very much like the one used today.   However, we used the term "sensation unit" because we thought it would require some education to have the term "decibel" adopted, and this proved to be the case.

"Being a clinical otologist I was, of course, trying to put into the audiometer everything I could think of at the time.   A main item was a receiver for each ear so that the sound could be switched for comparing the two ears, one with the other, without moving the receivers, and so that the sounds could be heard from both receivers simultaneously if desired. . . .

"Being the only one in possession of a dependable audiometer, I examined every patient, and a lot of nonpatients, to see what I could discover.   Most of my data simply confirmed quantitatively what we had known qualitatively before the advent of the audiometer, but now we could plot the threshold curve in definite units and at much smaller frequency intervals than before and I discovered in my deafened patients the narrow gaps, dips, etc., in the audiogram with which you are familiar.

"We used the two-decibel step in testing, but most patients did not detect even two decibel changes unless they had a neural deafness. This fact I discovered early and also the startling observation that in neural deafness there was a much greater increment of loudness with intensity than in normal ears or in impedance lesions.   For some time I thought this was an artefact, or that something was wrong with the audiometer, but it occurred so regularly in partial neural deafness that it could not be denied.   I coined the term "recruitment of loudness phenomenon" for this patho-physiological response. . . . I never found a lack of recruitment in neural deafness if the testing was properly done."

That, in substantially his own words, is the story of Dr. Fowler's discovery of the recruitment phenomenon and of the original Western Electric 1A audiometer. I have heard it said that Dr. Fowler was not the first to discover recruitment of loudness. I shall not debate this point. I do say that Dr. Fowler did discover or rediscover it for himself and that he is the man who "made it stick." Dr. Fowler comments on my rough draft, "do not put me on too high a pedestal in regard to the recruitment phenomenon because after all I blundered on it while definitely looking for something else."

Soon the simpler and more streamlined 2A audiometer was developed and others began using it to study both normal and abnormal hearing. For some time no one paid much attention to the phenomenon of "recruitment," perhaps because few otologists had audiometers with two receivers like the original 1A, but it is now recognized as an important diagnostic sign: a sure indication of sensory-neural impairment. It has also become a phenomenon of great theoretical interest and of importance to auditory neurophysiology and to psychoacoustics. Let me explain it a little more fully.

In a person with normal hearing a sound of the same physical intensity sounds equally loud in the two ears. If a person has a conductive hearing loss in one ear, the threshold is elevated by 10, 20, 30, or even as much as 60 decibels. The same difference that is measured at the threshold of hearing in the two ears also holds when the sound in the affected ear is adjusted to sound as loud to the subject as a comparison tone in the normal ear. If the threshold is elevated by 30 decibels, the difference revealed by the "loudness balance" between the two ears will also be 30 decibels. In most types of sensory-neural hearing loss, however, the difference between the hearing levels for the two ears, to give an equality of loudness between them, becomes less and less as we use more and more intense test tones. There may be perhaps a difference of 30 decibels in the thresholds for the two ears, but if the reference tone is raised to 80 decibels above the normal threshold it may be matched by a tone to the abnormal ear that is also 80 decibels above the normal threshold, not 110 decibels as it would be if the hearing loss were of the conductive type. In mathematical language we can say that the loudness in the abnormal ear has increased more rapidly than normal as a function of the intensity of the stimulus. It is this abnormally rapid increase, catching up, so to speak, with the normal ear, that led Dr. Fowler to choose the term "recruitment."

The phenomenon of recruitment is not yet understood in physiological terms although several hypotheses have been suggested. It has

forced us to think flexibly about the neurophysiological correlates of loudness, for its explanation must be included in any satisfactory theory of hearing. And from the audiological clinics has come ample confirmation of Fowler's very important additional observation that many ears that show recruitment have other defects of hearing also. A "pure" musical tone may sound rough, buzzing, or noisy, or it may sound like a mixture of two or more tones. Even more important, words do not "come clear." "I hear the sound," the patient says, "but I can't make out the words." In technical terms we say that his auditory discrimination is poor. This defect of hearing is quite different from mere elevation of the threshold for all or part of the acoustic spectrum. Like recruitment of loudness, it is particularly characteristic of disorders of the sensory apparatus within the cochlea. Like recruitment is not yet understood; and both phenomena tell us that auditory theories of previous generations have been far, far too simple!

One other study conducted in a hospital stands out as a fundamental contribution to the understanding of hearing. This is the clinical-pathological study at the Johns Hopkins Hospital carried out by Drs. Samuel Crowe, Stacy R. Guild, C. C. Bunch and L. M. Polvogt. Dr. Crowe, head of the Department of Otolaryngology, saw the necessity of correlating the pathology of the ear with clinical measurements of hearing. Dr. Guild was the anatomist, Dr. Bunch was what we would now call an audiologist, and Dr. Polvogt was a young clinical otologist. The hearing of thousands of hospital patients was measured, regardless of the disease from which they suffered, and hundreds of temporal bones were obtained at autopsy, properly fixed and decalcified, and ultimately examined microscopically. It was a monumental work, extending over many years. It illuminated the nature and revealed the incidence of "histological otosclerosis," that is, the presence in the bone of the otic capsule of the abnormal, vascularized "otosclerotic" areas and excrescences we have already mentioned. It confirmed the suspicion that "clinical otosclerosis" with hearing loss appears only when the footplate of the stapes becomes fixed or ankylosed, as we say, in the oval window.

But the most important finding of the study from the theoretical point of view was the demonstration of the pathology that is associated with abrupt high-tone hearing loss. By abrupt we do not mean sudden in onset of the disease, but abrupt in the sense of a sharp cut-off on the frequency scale. Tones up to 2000, 3000, or 4000 cycles per second are heard quite well but those above the cut-off are heard very poorly or not at all. Such abrupt high-tone loss turned out to be associated clearly and unmistakably with degeneration of sensory cells,

and usually of the nerve fibers as well, in the basal turn of the cochlea. The farther down the scale the hearing loss extended the farther along the basilar membrane did the atrophy of sensory and neural tissue extend. In fact a statistical analysis of the relation of the extent of the lesion to the audiograms has defined, within rather narrow limits, the positions on the basilar membrane where normal cells must be present if the particular frequencies of 2000, 4000, and 8000 cycles per second are to be heard by the human ear.

The relation of frequency to position along the basilar membrane was not a new idea. It was a fundamental part of the resonance theory as elaborated by Helmholtz. Several other lines of evidence, including psychoacoustics and electrophysiology, converged to support this concept, but the findings of Guild and his collaborators stand out as a *direct* demonstration of this principle in *human* hearing.

Guild also noted that corresponding severe but sharply limited degenerations in the middle and apical regions were much rarer than those in the basal turn. Why this should be is still a puzzle. He also pointed out that the clear correlation between place and frequency, seen so well for high tones, does not hold for low tones. Low tones seem to be heard, somehow, throughout the cochlea. This conclusion emerged quite clearly from Guild's analysis of the audiograms of patients in whom Dr. Dandy had partially but not completely severed the cochlear part of the auditory nerve while sectioning the vestibular part for the relief of the symptoms of Ménière's disease. Whatever part of the nerve was cut, as described in Dr. Dandy's operative notes, hearing for low tones remained, although hearing for high tones was nearly always impaired and approximately in proportion to the percentage of fibers cut.

A very recent report from Holland by Dr. Gravendeel of more than forty cases with what Dr. Gravendeel calls perceptive "bass deafness" leaves me with an impression like Dr. Guild's review of Dr. Dandy's cases. His patients respond to tones below 1000 or perhaps 500 cycles per second but these thresholds are considerably elevated and the cut-off in some cases is very sharp indeed, just as it is in abrupt high-tone deafness. Dr. Gravendeel concludes that many of his patients really did not hear the low tones at all but only their higher harmonics, to which the ear is normally far more sensitive. Often the quality of the low tones was rough and buzzing and sometimes the pitch was false. This last symptom is known as diplacusis. Dr. Gravendeel gives some fairly good reasons for believing that his patients do not have an abnormality of the cochlear but that the trouble lies in

the brain stem. His theoretical suggestion of an abnormal inhibitory action of the brain stem on the cochlea is implausible to say the least, but so is any other single simple explanation. Many details of his cases, as well as of Dr. Dandy's cases, cannot yet be explained, but the observations are important demonstrations of the complexity of the auditory mechanism.

A factor common to both sets of cases is the evident widespread activation of the cochlea by low-frequency sound. Such a widespread activation has been observed visually by von Békésy and also demonstrated by our own electrical recording; and von Békésy and others have given full explanations in terms of the physical principles of resonant vibration. Electrophysiological studies of the discharge of impulses in the auditory nerve have further established the frequency principle of Rutherford, including the volley theory of Wever, as a correct partial description of the pattern of nerve impulses sent up the auditory nerve in response to low-frequency sounds. Some information about the frequency of a low tone is transmitted in the form of the frequency of successive volleys of nerve impulses. This fact will probably account for some of the puzzles posed by clinical studies of "bass deafness" and of damage to the auditory nerve. Acoustic analysis and the place principle of Helmholtz are not the entire story.

Clinical and pathological studies did not in themselves establish the frequency principle, but they did correctly give warning, so to speak, that the auditory mechanism of the ear and the psychological and physiological processes of hearing are very complicated indeed. Much, much work remains to be done, and it is quite evident that well planned and carefully conducted studies of diseased ears and injured brains in the clinic can contribute greatly, and perhaps even more than they have in the past, to the understanding of hearing.

As we move from the ear to the brain, I must mention a very noteworthy observation made in 1927-28 by Dr. C. C. Bunch. During his audiometric survey at the Johns Hopkins Hospital he tested the hearing of a woman whose entire right cerebral hemisphere had been removed, because of invading malignancy, by Dr. W. E. Dandy. To the surprise of Drs. Bunch and Guild, the woman's audiograms were practically identical for the right and left ears. All frequencies were heard, and, allowing for restrictions in the application of the receiver to the head, were within normal limits of sensitivity. The point here is the equal representation of the two ears in one cerebral hemisphere and, by inference, the bilateral representation of each ear. As far as I am aware, this is the first direct demonstration in man of

substantially equal bilateral representation in the central auditory system.

   Actually, some very important insight into certain fundamentals of hearing at the psychological level has come from the clinical study of the symptoms of auditory agnosia and aphasia. These terms refer to loss of understanding of the meaning of words. In auditory agnosia the ear still sends impulses up the auditory nerve but the patient pays little attention or simply does not understand the meaning of the auditory signals and symbols. Children who suffer from this condition as a result of faulty development or accident at birth often appear to be deaf. This condition, which I call "auditory agnosia," is the sensory counterpart of the inability to name objects or, in general, to find the words to express ideas in speech. The latter condition is properly called "expressive aphasia." Unfortunately, the use of the word "aphasia" has now spread widely to include almost any disorder of the ability to use or understand symbols. My point, however, is not a semantic quarrel but the simple statement that if it had not been for the clinical study of adults with obvious injuries to the brain and of children who did not learn to talk because they could not learn the meaning of the sounds that they heard, we would know far less than we do today about the central auditory functions and the psychology of hearing. From the way in which the auditory, the perceptive, and the cognitive functions break down and go wrong when the brain is injured or fails to develop normally, and from the success or failure of various empirical methods of teaching and rehabilitating, we now know something of the central aspects of auditory communication in its broadest sense.

   I shall not attempt to give specific examples or to analyze further the problems of agnosia and aphasia. They lead us to the very difficult area where psychology and neurophysiology meet in what one calls the mind and the other the brain. But perhaps in the work of Wilder Penfield and his associates we have already had a glimpse of a golden future in the study of cerebral mechanisms of hearing. Dr. Penfield has stimulated locally the brains of conscious patients on the operating table. When he stimulated the temporal lobe of certain epileptic brains, a train of memory was started. Whole conversations or musical tunes, fully played out in time, passed through the patients' minds as a revived auditory memory. This is certainly a fundamental contribution.

   These are some of the highlights of the last half century in the advancement of knowledge in the basic sciences that have originated

in problems or observations in otology. In some other branches of medicine or surgery the links between the clinic and the operating room on the one hand and the laboratory of basic science on the other may be closer or the flow of information and inspiration in each direction may be more obvious, but it is clear that otology too has made its share of contributions to basic knowledge.

818 S. KINGSHIGHWAY

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THE PAROTID COMPARTMENT

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The parotid compartment is a region of concern to the clinician because of the involvement of the parotid gland in benign and malignant tumors necessitating surgical intervention. In this event, a knowledge of the anatomy of the gland, facial nerve, and vascular contents of the compartment becomes essential. In cases of pyogenic infections of the compartment it is important that we have a clear understanding of the fascial envelope enclosing the region. This knowledge is essential if we are to intelligently anticipate the spread of purulent fluids from the parotid compartment to contiguous potential spaces containing vital structures and vice versa. Despite the fact that man has been operating in this region before the latter part of the seventeenth century, the present study has revealed certain information on the fascial boundaries, contents, and relations which, to our knowledge, has not been previously reported. It is my purpose to try to present this information to the reader in a logical and coherent fashion with the hope that it may benefit the clinician and the academician.

The parotid compartment is a circumscribed region of the head which is delimited by fasciae and contains the parotid gland, nerves, vessels, and lymphatics. The following descriptions are based on the author's dissections of 40 half heads and the observations made of several hundred student dissections of the region.

THE PERIPAROTID FASCIA

This fascia forms a posteromedial, an anteromedial, a superior, and a lateral wall of the compartment. The anteromedial and posteromedial walls converge internally on the basal two-thirds of the

styloid process and, below this, on the fascia covering the lateral sur-
face of the stylopharyngeus muscle.

The lateral wall or superficial stratum of periparotid fascia is
continuous with the lateral lips of the other walls (Figs. 1-4).   The
anteromedial wall continues anteriorly beyond the posterior border
of the ramus to fuse with the masseteric fascia and accommodates an
anterior extension of the superficial portion of the gland before
becoming confluent with the superficial stratum.   Posteriorly, the
superficial and deep parts of the periparotid fascia become continuous
near the anterior border of the sternocleidomastoid muscle.   Inferi-
orly, the superficial stratum blends with the anteromedial and postero-
medial walls to house a cervical extension of the parotid gland.   In
the cadaver, the superficial layer adheres intimately to the overlying
platysma muscle and can be separated only by careful dissection.
Furthermore, over the posterolateral part of the gland, in the pre-
auricular area, the superficial stratum becomes thin and indistinct,
generally making complete removal impossible.   Nevertheless, this
superficial layer of periparotid fascia, in addition to the subcutaneous
connective tissue, does exist.   It is not, however, as described by
Ford,[13] "a sheet of fibrous tissue as tough as whip cord."

The superior wall of the parotid compartment is formed by the
inferior and anterior portions of the cartilaginous external auditory
meatus, the stylomastoid fossa, the postglenoid spine, and the postero-
lateral one-third, approximately, of the tympanic part of the temporal
bone (Figs. 1 and 7).   The region is covered by a thin layer of fascia
which passes over smoothly into the lateral, anteromedial and postero-
medial walls.

The posteromedial wall (Figs. 1-7) is a fascia of varying regional
density which extends laterally from the styloid process to the sterno-
cleidomastoid muscle.   The portion of this sheet which passes from
the styloid process to the stylohyoid muscle is a thin but distinct plane.
It presents a foramen for the passage of the external carotid artery
and its accompanying vein.   This fascia encloses the stylohoid muscle
and continues to the posterior belly of the digastric as a dense layer.
Occasionally this layer is pierced by the external carotid and the
posterior auricular arteries.   Such a perforation occurs when the
external carotid enters the compartment below the stylohoid muscle
and the posterior auricular artery originates deep to the compartment.
After completely investing the posterior digastric muscle, the fascia
continues laterally to enclose the sternocleidomastoid muscle.   In the
region of the mastoid process there may be a pocket between the adja-

cent surfaces of the digastric and sternocleidomastoid to accommodate a posterior process of the parotid gland. From the lateral surface of the anterior third of the sternocleidomastoid muscle the fascia becomes continuous with the superficial stratum of periparotid fascia.

The anteromedial wall extends from the styloid process and, below this, the fascia on the lateral surface of the stylopharyngeus muscle to the posterior border of the mandible. This is a complete fascial plane which contains the stylohyoid ligament and the styloglossus muscle. Superiorly, it is attached to the tympanic part of the temporal bone along a line extending from the styloid root to the notch between the tympanic ring and retroarticular tubercle. The portion of this sheet extending from the styloid process to the posterior border of the mandible has been designated by Scheldrup[44] as the stylomandibular membrane.

The portion of the anteromedial wall reaching from the lateral surface of the stylopharyngeus muscle to the posterior border of the stylomandibular membrane participates in the medial wall of the fossa only as far inferiorly as the entrance of the external carotid artery into the compartment. In this vicinity the stylopharyngeus muscle passes deep to the medial wall and the fascia continues inferiorly to sweep between the posterior border of the stylomandibular membrane and the stylohyoid muscle. Within this membrane a thickening, the stylomandibular ligament, reaches from the styloid process (at the junction of its middle and lower third) to the posterior border of the ramus. Its attachment to the ramus extends superiorly from the angle for a distance of one or two centimeters. The thinner portion of the membrane extends between the base of the skull, the styloid process, the superior edge of the stylomandibular ligament, and the posterior border of the ramus (Figs. 2, 5 and 6). It has been identified as the stylomandibular fascia by Gaughran.[17] The area occupied by the stylomandibular fascia has been designated the *orifice préstylien* by Faure,[12] *boutonnière rétrocondylienne* by Rouviere,[42] and the stylomandibular tunnel by Patey and Thackray.[35] Some workers indicated this opening to be a direct communication between the parotid compartment and the lateral pharyngeal cleft.[25,32,46,51] Other researchers considered this area to be closed by a *lame fibreuse*,[6] an *apon. parot. (partie mince)*,[42] or an *aponeurose stylomaxillaire*.[24] There is not, even today, general agreement concerning the presence or character of a stylomandibular fascia. Nevertheless, such a fascia is always present. It is thin and cribriform when a stylomandibular process of the parotid gland is present, but dense when this process is absent. This fascia presents a barrier of varying effectiveness against
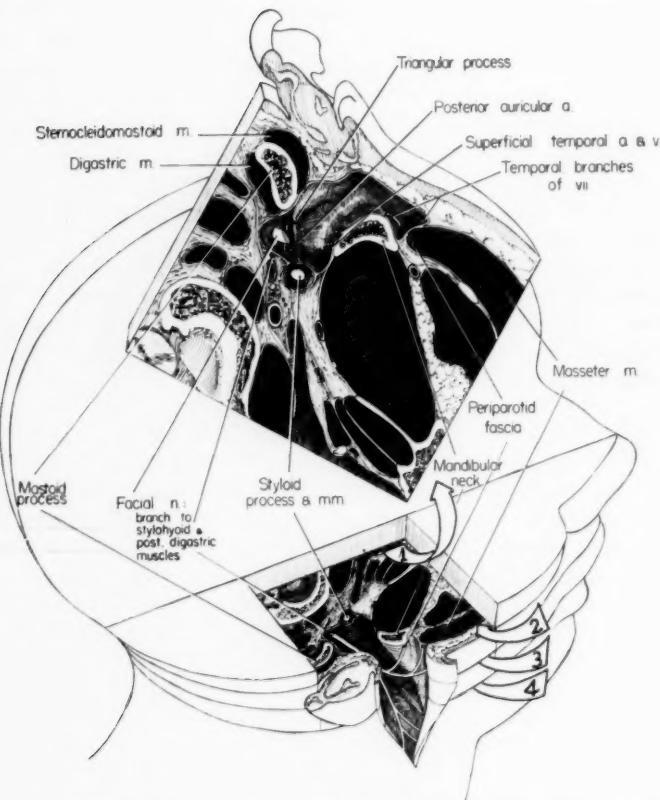
Fig. 1.—An orientation sketch of a series of cross sections through the parotid compartment. Section 1, turned upward and enlarged, shows the roof of the parotid compartment.

the passage of fluid between the parotid compartment, the lateral pharyngeal cleft, and the masticator compartment.

The stylomandibular ligament does not, as stated in our standard reference texts (Gray, Morris, and Cunningham), act as a partition between the parotid and the submandibular gland. There is, however, a band of fascia, not generally recognized in this country, which passes from the region of the mandibular angle posteroinferiorly to the posterior digastric and sternocleidomastoid muscles. This band of fascia will be designated here as the "interglandular septum." It was
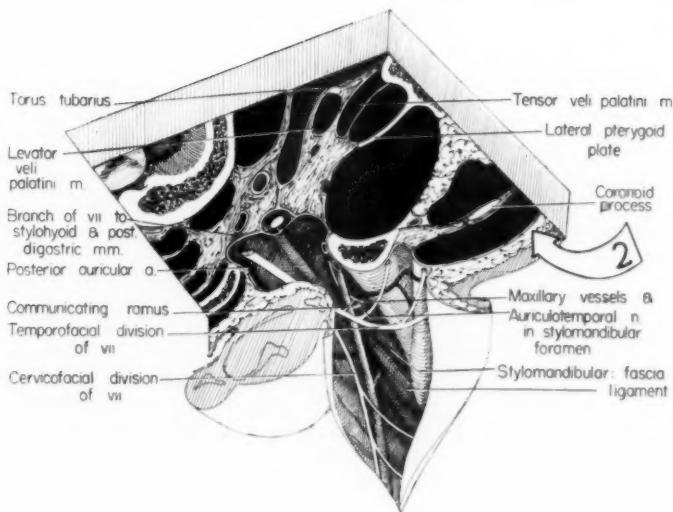
Fig. 2.—An enlargement of the section shown at level 2 in Figure 1 and viewed from above. The two divisions of the facial nerve are visible. One communicating ramus is shown in the region of the maxillary vessels, passing between the temporofacial division and the auriculotemporal nerve.

described in 1883 in the living subject by Burns.[5]   In fact, as is true of the pterygomandibular raphe, it is better demonstrated in the surface anatomy of the living than in cadaver dissection. The septum continues superiorly with the sheet of fascia extending between the stylomandibular ligament and the stylohyoid muscle, inferiorly with the superficial lamina of parotid fascia, anteriorly with the masseteric fascia, and posteriorly with the posterior digastric and sternocleido-mastoid muscle sheaths. It may exhibit a falciform edge along the antero-inferior margin of the point of entrance of the external carotid artery into the parotid compartment.

Other terms used to identify the interglandular septum are: *pars angularis fasciae colli*, *bandelette maxillaire*, and *cintilla intermaxilo-parotidea*. In the English speaking countries, Meyers[29] and Stranc[47] recognized that this fascial specialization separated the parotid from the submandibular gland. In the United States, the few workers who do recognize this structure, have anglicized the *pars angularis* to angular tract.

TABLE I

LENGTH OF STYLOID PROCESSES MEASURED
IN 153 DISSECTED HALF HEADS*

LENGTH IN MM	NUMBER OF SPECIMENS
1 - 9.9	6
10 - 19.9	35
20 - 29.9	80
30 - 39.9	23
40 - 49.9	5
50 - 59.9	1
60 - 69.9	1
70 - 79.9	2

*Measurements were made from the point at which the styloid process projects beyond the inferior edge of the vaginal process of the tympanic part of the temporal bone.

The styloid process, as mentioned earlier, forms one of the boundaries of the parotid compartment. Being a firm, palpable structure, some clinicians have used this process as a landmark in parotid surgery. Recently, Davis et al.,[10] on the basis of an osteological study, indicated that the styloid process is unreliable as a skeletal landmark. This report states that the process was "wholly absent in 58 of the 150 cranial halves examined, but shielded by the vagina processus styloidei in more than 40 others." This would mean that the styloid process was not palpable in at least one-half of the specimens. A subsequent report on the surgery of the parotid gland, cited these data. I have examined 194 half heads, representing both personal dissections and student laboratory dissections. Of this number, 193 had styloid processes which projected beyond the vaginal plate. Processes were measured in 153 of the above number and the results are shown in Table I. Thirteen half heads (almost 9%) showed fibrous cartilaginous bases which could be lost in cleaning and which were sufficiently mobile as to possibly escape palpation. The shortest process was 2.0 mm and the longest was 74.0 mm. Fifty-seven per cent of the styloid processes were between 20.0 and 29.9 mm. Fritz[14] stated that normal styloids range between 2.5 and 3.0 centimeters in length. I feel that an erroneous impression was obtained by Davis and his colleagues as a result of their study of dried osteological specimens and wish to emphasize that the styloid process is a reliable skeletal landmark.

CONTENTS OF THE PAROTID COMPARTMENT

One of the most important constituents of the parotid compartment is the facial nerve. Here a knowledge of its exit, course, and relations is of the utmost importance to the surgeon working in this area. It is essential to be able to locate this nerve rapidly and safely not only in the extirpation of the parotid gland but also in the approach to the glossopharyngeal nerve as outlined by Welti and Chavany.[52] Some workers have approached the facial nerve from its terminal rami, tracing these centripetally to the main trunk. Others have attempted to locate the trunk of the facial nerve and trace this forward to its various divisions.

Utilizing the latter method, surgeons have employed various landmarks, such as the stylomandibular artery, the mastoid process, and the styloid process, as aids in the identification of the root of the VII cranial nerve. On the basis of personal dissections, the present writer considers the following to be a rapid and safe technique for locating the facial nerve after its emergence from the stylomastoid foramen. One first frees the gland along the anteroinferior wall of the external auditory meatus. This is readily accomplished since the attachment of the gland is loose in this area. Working deep to the fossa, immediately anterior to the mastoid process, one finds a triangular shaped process of cartilage with its apex directed medially (Figs. 1 and 7). This is the triangular process of the cartilaginous external auditory meatus. Its apex points to the anterior border of the VII nerve as it emerges from the stylomastoid foramen. Gutierrez[21] in an investigation of the parotid region illustrates this process and labels it a spur (*agujero*) of the external auditory conduit. His text, however, does not mention its significance in locating the VII nerve.

Arising from the trunk of the facial nerve, prior to its temporal and cervical bifurcation, are the posterior auricular nerve and the nerve to the posterior digastric and stylohyoid muscles. The operator should have some knowledge of the location of these branches. Pilheu[38] stated that the branches to the stylohyoid and posterior digastric were in the parotid compartment. Actually, however, all three of these nerves are medial to or within the posteromedial fascial floor (Figs. 1 and 2) and are not in danger of being damaged if the surgeon remains within the compartment.

After giving off the aforementioned branches, the facial nerve enters the parotid gland. Davis *et al.*[10] stated that the average distance of bifurcation of the facial nerve into its two divisions was superiorly two-thirds of the distance from the angle of the mandible
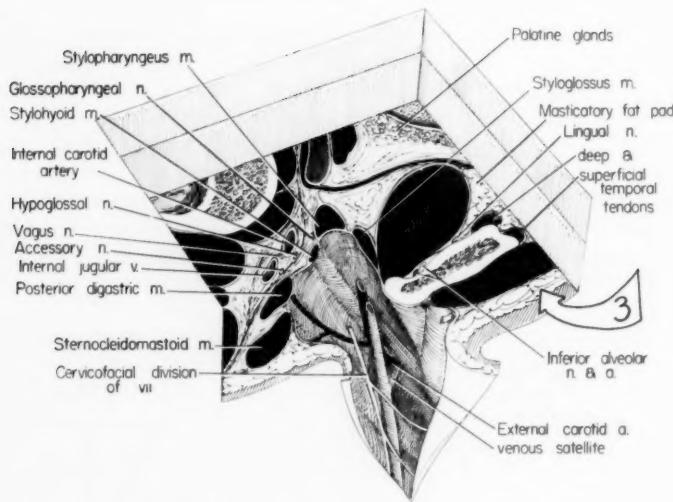
Fig. 3.—A section taken at level three as indicated in the orientation sketch. The entrance of the external carotid artery and the exit of a satellite vein are visible above the stylohyoid muscle.

to the temporomandibular joint. This condition was observed in 75% of my specimens. Pilheu[38] indicated a bifurcation in the upper third of the distance in only 25% of the specimens which he dissected. He stated further that the facial nerve showed a trifurcation in 15% of the heads (6 out of 40 cases), whereas Davis indicated a 100% bifurcation. The subdivision of the temporofacial and cervicofacial divisions may be so close to the point of original bifurcation as to be interpreted as a trifurcated condition. In fact, of the 61 specimens which were examined in my series, three half heads (about 5%) showed an early separation of the buccal ramus very close to the primary division point of the facial nerve trunk.

An important point, yet one that is ignored in recent reports on parotid gland surgery, are the communications between the auriculotemporal branch of the trigeminal nerve and the facial nerve (Figs. 2 and 5). These communicating rami are not a recent finding. They were described by Cloquet in 1822,[7] and this is probably not their first description. Riessner[41] referred to these branches as the anastomotic part of the auriculotemporal nerve and recommended cutting them to make the formation of postoperative fistulas impossible. I

stress these anastomoses because they effectively anchor the root of the temporofacial division, definitely interfering with its mobilization. These communicating rami were present in all the heads examined and in all cases were between the auriculotemporal nerve and the temporofacial division or its rami. The communicating rami are located in the region of, or immediately above, the maxillary vessels. Most frequently, branches pass posterior to the mandibular ramus but anterior to the external carotid and the superficial temporal arteries. These rami may also pass posterior to both of the vessels or between the artery and the retromandibular vein. The number of communicating rami varies from one to four, the average number being two. Intraglandular anastomotic rami are encountered between the great auricular and the facial nerve and between the transverse cervical and the facial nerve.

The pattern and number of the rami formed by the temporofacial and cervicofacial divisions of the nerve have been presented by McCormack et al.[28] and Davis et al.[10] One very important point of which the surgeon must be aware, however, is that all facial nerve rami are not in the same sagittal plane. This is not clearly expressed in most present day reports.

The largest constituent of the parotid compartment is the parotid gland. Considerable discussion has centered on its lobular character. Is this gland bilobed or unilobar? The greater number of workers have supported the bilobular concept. Bailey[3] made repeated, urgent requests for the anatomist to consider the gland to be formed of a comparatively large superficial lobe and and a variably sized deep lobe connected by an isthmus and with the facial nerve rami lying in an interlobar plane. The present writer confirms the concept of the facial nerve rami lying in loose connective tissue in which they can be followed backward to the cervicofacial and temporofacial divisions, and the root of the facial nerve. As mentioned earlier, however, all of these rami cannot be found in the same sagittal plane and do not separate the gland into superficial and deep lobes.

Riessner[41] expressed difficulty in recognizing the bilobed structure of the parotid in operative and cadaver material. Rouviere and Cordier[43] indicated several deep lobules connected to a superficial lobe by several isthmi. Audouin and Neveu[2] described bridges between a superficial and a deep part of the gland. Hurford[23] had difficulty demonstrating superficial and deep lobes connected by an isthmus. Pilheu[38] also described many bridges connecting a large superficial and small deep lobe. More recently, Winsten and Ward[53] using an injection-corrosion technique, described the parotid as unilobar.
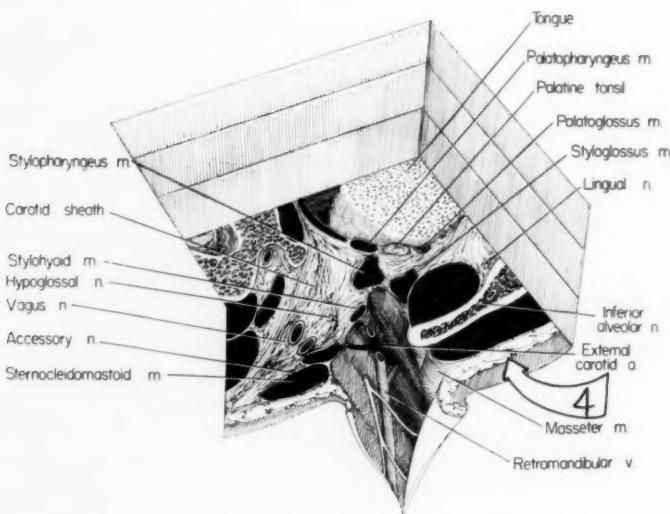
Fig. 4.—Section number four, taken from Figure 1, showing the lower pole of the parotid campartment.

Careful dissections of the parotid gland fail to demonstrate with any degree of satisfaction clearly superficial and deep lobes connected by one isthmus. It is perhaps better to describe the parotid as a unilobar gland which, in its development, has enveloped certain neurovascular structures. We can, nevertheless, recognize superficial and deep portions. This is in agreement with the terminology adopted by the International Anatomical Nomenclature Commission (1955). Patey and Ranger[36] have described a faciovenous plane along the course of the superficial temporal and retromandibular veins. These veins were said to form a plexus deep to the facial nerve and its branches, though exceptionally, certain branches of the nerve passed deep to the veins. This plane is readily identified in the cadaver and can be used, as they stated, to assist in locating the plane of the facial nerve. One should remember, however, that it is not unusual to find some rami of the inferior division as well as temporal and zygomatic rami passing deep to the venous network.

The general shape of the gland is well known and has been redescribed by McCormack et al.[28] However, there are a number of glandular processes which should be considered because of their relations and possible significance. From the superficial portion of the

gland there may be extensions of a condylar, a meatal, or a posterior process. The condylar process is usually a thin mass of parotid tissue located medial to the temporofacial nerve rami and concealing the temporomandibular joint and the base of the transverse facial vessels. The meatal process, rare in occurrence, rests in the meatal incisure of the cartilaginous external acoustic meatus. The posterior process projects dorsally between the mastoid process of the skull and the sterno-cleidomastoid muscle and, inferior to the apex of the mastoid, between the digastric and the sternocleidomastoid muscle. It varies in length from several millimeters to two centimeters. Pilheu[38] recorded a tongue of gland in this position in 20% of his specimens. On the basis of the present study, its occurrence appears to be more frequent than this. The posterior process is just lateral to the internal jugular vein and the latter is particularly vulnerable to erosion from an infection of this process of the parotid gland.

The deep part of the parotid, medial to the mandibular ramus, exhibits a glenoid and a stylomandibular process. In addition to these projections, Parsons[34] has described a pterygoid process resting on the superficial surface of the medial pterygoid muscle. Symington[48] placed this process on the deep surface of the same muscle and Redon[40] described a pterygoid process accompanying the maxillary artery. The present observations could not confirm the existence of any pterygoid processes. The glenoid process is a small projection which rests on the vaginal process of the tympanic part of the temporal bone. It does not enter the mandibular fossa and conceals but a portion of the vaginal plate.

The stylomandibular process projects anteromedialward above the superior edge of the stylomandibular ligament. It rests on the anterior surface of the styloid process and, more medially, lies anterior to the internal carotid artery. The external carotid artery, as it ascends, loops around the posterior border of the neck of the process. This portion of the gland has been identified as the carotid lobe by Furstenberg[15] and as a pharyngeal extension by Faure.[12] The former name is more appropriate. The latter is misleading because the process does not have a close relationship to the pharynx wall. The term stylomandibular process was adopted by the present writer since this process pushes anteriorly into the fascia of the same name. Some workers indicated that they had never seen this deep process but others have reported its presence. More precise data on the presence of the process, given as percentage occurrence, are: Trolard[50] - 0%, Gilis and Peyron[18] - 12.5%, Costantini[8] - 33%, Testut and Latarjet[49] - 70 to 80%, and Winsten and Ward[53] - 100%. My examina-
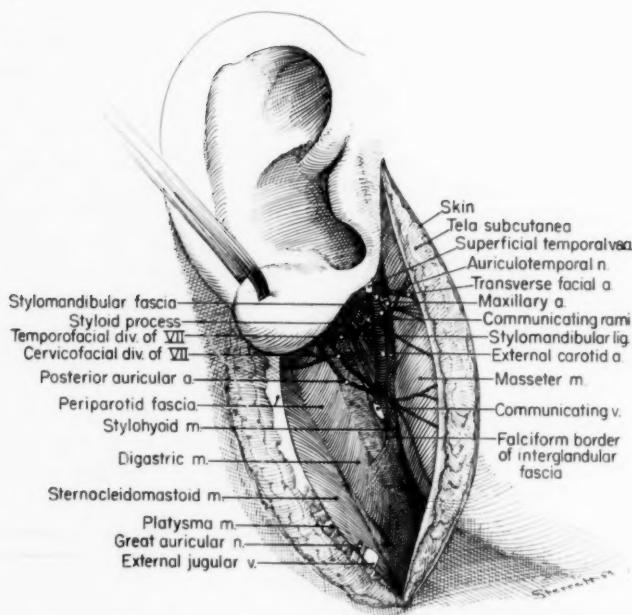
Fig. 5.—A lateral view of a dissection of the right parotid compartment showing the anteromedial and posteromedial walls together with most of the neurovascular structures.

tion of 154 half heads has shown a stylomandibular process to be present in 74% of the specimens. It lies immediately adjacent to the lateral pharyngeal cleft but is separated from it by the thin stylomandibular fascia (Figs. 6 and 7).

Tumors of the stylomandibular process of the parotid gland have been reported by Perier,[37] Mixter,[30] Sertoli,[45] Proby,[39] and others. Faure[12] described a technique involving resection of the mandibular ramus for the removal of a tumor of the deep process. Leriche[27] and Morfit[31] discussed a submandibular approach to a tumor of the stylomandibular process. Patey and Thackray[35] described a superficial approach in which they transected the stylomandibular ligament and fractured the styloid process in order to remove such a tumor. Ehrlich[11] utilized an intraoral approach for the excision of this deep parotid tumor. Wise and Baker[54] removed the superficial portion of the gland and, elevating the facial nerve rami superiorly, delivered the

deep tumor inferiorly into the neck. The frequent occurrence of the stylomandibular process of the parotid gland, its proximity to the pharynx, its contiguity with the lateral pharyngeal cleft, and its intimate relationship to the external carotid artery make tumors of this process particularly significant.

Of the arterial contents of the parotid compartment, the largest and mother trunk of the vessels to be described is the external carotid artery. It is located in the depths of the fossa and is usually not completely enclosed in parotid tissue but rather, rests in a gutter on the medial surface of the gland or simply rests in contact with the medial surface. If one places a straight edge on the surface of the skin with its upper edge passing from the mastoid apex to the mandibular angle (angulo-mastoid line), the external carotid artery enters the parotid compartment above this edge. Occasionally the external carotid artery enters the parotid compartment between the stylohyoid and the posterior digastric muscles rather than above the former muscle (Figs. 2-5). This condition was seen in two specimens among 72 half heads. Gruber[20] cited one case of this relationship, and stated that Quain had found only three examples out of 291 cadavers. Adachi[1] cited three cases among 141 half heads in which the external carotid artery passed between the posterior digastric and stylohyoid muscles.

The first branch of the external carotid in the parotid compartment is the posterior auricular artery. It usually passes postero-superiorly deep to the root of the facial nerve between the medial aspect of the gland and the fascial floor (Figs. 2 and 5). The posterior auricular artery normally arises from the external carotid just inside the parotid fossa. However, in 6 out of 50 half heads, it came off deep to the fascial wall of the fossa and entered between the digastric and stylohyoid muscles. In these instances the artery entered the fossa closer to the base of the styloid process. In two specimens of the 50 the posterior auricular artery was given off from the occipital artery. The posterior auricular artery may be encountered passing posteriorly, lateral to the trunk of the facial nerve. This condition was observed in 5 out of 46 half heads dissected. Infrequently the posterior auricular artery passes through a split in the root of the facial nerve. Its auricular branch is located at the anterior border of the mastoid process together with a branch of the great auricular nerve. Its stylomastoid branch usually passes deep to the VII nerve as it enters the stylomastoid foramen, though it was seen to be superficial to the nerve in one specimen.
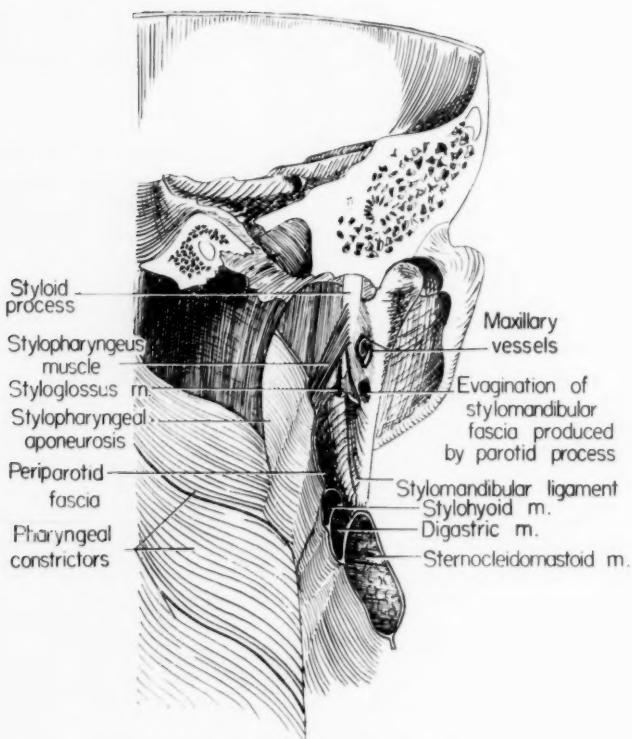
Fig. 6.—A posterior view of the head, sectioned frontally just behind the temporomandibular joint, to show the location of the fascial pocket which accommodates the stylomandibular process of the parotid gland.

The external carotid artery arches upward around the posterior border of the neck of the stylomandibular process of the gland to bifurcate into the maxillary and superficial temporal arteries. The intimate relationship of the external carotid artery to the stylomandibular process places the vessel in danger of being injured in the removal of deep process tumors. The maxillary artery leaves the fossa by passing forward through the stylomandibular fascia and the tympanomandibular ligament to enter the masticator space.[16] From this vessel a small artery, the deep auricular, passes posteriorly to course through the upper part of the parotid compartment or through the fascial roof. With the artery is the meatal branch of

the auriculotemporal nerve. Above the level of the maxillary artery, the terminal part of the external carotid, the superficial temporal, continues upward with its satellite vein and the auriculotemporal nerve to leave the fossa at the level of the zygomatic arch. The transverse facial artery arises from the superficial temporal artery. The transverse facial artery is usually not within the parotid gland although it is within the compartment; it passes forward curving around the posterior ramal border in the region of the mandibular notch. The transverse facial artery generally gives rise to a sizeable masseteric branch (superficial masseteric artery of Ohlweiler). In addition to the above branches, are numerous parotid twigs from the external carotid which enter the substance of the gland and distribute within the parotid compartment. On the basis of a study by Ohl-weiler,[33] these vary from 9 to 17.

The veins located within the parotid fossa are the superficial temporal, transverse facial, maxillary, retromandibular with its anteri-or and posterior divisions, posterior auricular, and the external jugular (Figs. 2 and 5). The most common venous arrangement was a bifur-cation of the retromandibular vein. The posterior division joined a posterior auricular vein to form the external jugular. The anterior division either passed through the periparotid fascia, accompanying the external carotid artery, to join the facial vein or emptied into the internal jugular directly. In some specimens both of these channels were present. The veins were usually superficial to most or all of the rami of the facial nerve, but it was not exceptional to find several rami passing deep to the veins. An anastomotic branch between the transverse cervical and the cervical branch of the facial nerve usually accompanied the external jugular vein.

Subfascial and intraglandular parotid lymph nodes were observed but details of number, location, and drainage were not determined.

COMMENT

The spread of a purulent fluid from the parotid compartment to adjacent regions bears a direct relationship to the completeness and density of the periparotid envelope. This envelope is complete, but an area of weakness may exist in the anteromedial wall. In a small percent of cases there is no stylomandibular process of the parotid gland and the anteromedial wall is dense; it then forms an effective barrier between the parotid compartment and the lateral pharyngeal cleft. In the majority of cases, however, this process is well developed and pushes forward into the stylomandibular fascia, resulting in a
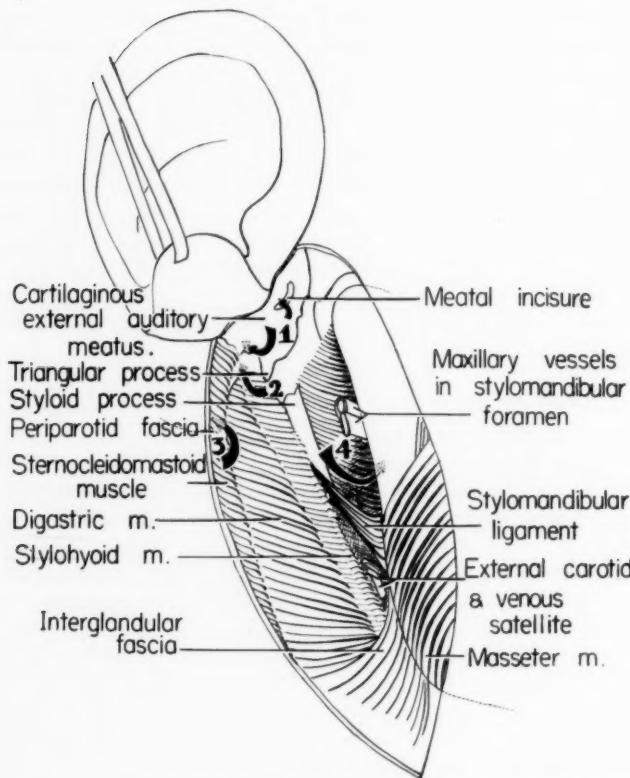
Fig. 7.—A lateral view of the right side of the head to show the parotid fossa. The black arrows indicate the positions occupied by various processes of the gland: 1) meatal, 2) stylomastoid, 3) posterior, and 4) stylomandibular process.

thin, cribriform lamella. These conditions explain the seemingly contradictory statements concerning the passage of fluid from the parotid compartment to the lateral pharyngeal cleft. On the basis of these data it is wise to assume the likelihood of fluid spread between the two regions. Posteriorly, the anterior wall of the cartilaginous external auditory meatus presents a weak area at the meatal incisures. In addition, a potential weak spot in the fascial pocket accommodating the posterior process of the gland may offer an avenue for infection to reach the lateral wall of the carotid sheath and the internal jugular vein. Grodinsky and Holyoke[19] reported that fluid injected into the

parotid compartment was also seen to rupture into the masticator and the submandibular compartments. Spread into the masticator compartment would probably follow the route of the maxillary vessels rather than penetrate both the stylomandibular fascia and the tympanomandibular portion of the interpterygoid fascia. On the basis of fascial densities, it is most likely that fluids will penetrate the anteromedial wall of the parotid region to enter the lateral pharyngeal cleft. This is in itself, however, a very critical point. As described in an earlier report[17] the lateral pharyngeal cleft lies directly adjacent to seven potential spaces. Fascial densities are, of course, not the only factor to be considered in the spread of fluids. Additional significant factors are: the location of the fluid, the elasticity of the surrounding structures, and even the massaging action of the mandible and surrounding muscles.

The performance of the first parotidectomy has been variously reported by different writers. Heister[22] stated that parotid extirpations were executed by the Dutch before the year 1693. As parotid surgery progressed it became more and more apparent that the earlier technique of simple tumor enucleation was inadequate and constituted merely a palliative measure. Many workers recommend the radical excision of parotid tumors. This raises a question of the feasibility of a complete extirpation of the parotid. Figure 7 illustrates some of the processes of the gland which can be encountered. Most of these are tucked in devious corners of the compartment; their presence is not particularly apparent and their extraction is questionable.

In the process of removing the parotid, the surgeon needs a simple, reliable, and rapid approach to the facial nerve trunk. With this in mind, Courriades and Rigaud[9] recommended using the stylomastoid artery as a landmark; Lathrop[26] suggested the use of the styloid process, and Beahrs and Adson[4] advised using the mastoid process. Though the proper use of any of these landmarks will lead the operator to the facial nerve, the technique outlined earlier in this paper is a rapid and reliable means of locating the nerve. This technique involves working along the portion of the gland bordering the cartilaginous external auditory meatus to locate the triangular process of cartilage. The apex of this process is directed toward the anterior border of the VII nerve. This approach to the root of the VII cranial nerve is recommended to the surgeon for his consideration and evaluation.

An additional point of interest to the surgeon is the presence of communicating rami between the auriculotemporal nerve and the temporofacial division of the facial nerve. These rami act to effec-

tively anchor this division and limit its maneuverability. The operator should be cautioned, however, that these communicating branches are located in the region of the posterior border of the mandibular ramus at the horizontal level of the transverse facial and maxillary vessels. The latter vessel constitutes a potential hazard since it has but a short course in the parotid compartment and, if sectioned inadvertently, may be difficult to ligate. The external carotid artery can be located and ligated as it enters the compartment above the angulomastoid line. It has been suggested in the surgical literature, however, that in routine parotid resection the external carotid artery should not be ligated in case a radical neck dissection has to be done at a later date.

SUMMARY

The parotid gland is enclosed in a fascial envelope which, although complete, usually has a cribriform zone in the stylomandibular portion of the fascia. A portion of this parotid envelope, the interglandular fascia, separates the parotid from the submandibular gland. The parotid is best considered a unilobar gland in which can be recognized deep and superficial portions. The parotid has small processes extending into the various corners of the compartment, making it extremely difficult to be positive of a complete excision of the gland. A frequently occurring stylomandibular process should be approached with respect and enucleated with discretion because of its vascular and spatial relationships. Other processes to be looked for are the meatal, glenoid, condylar, and posterior. The root of the facial nerve can be located rapidly and safely by using the triangular process of the cartilaginous auditory meatus as a landmark. The branches of this nerve to the stylohyoid and posterior digastric muscles as well as the posterior auricular nerve are not within the parotid compartment. An operator should keep in mind the one to four communicating branches between the auriculotemporal nerve and the temporofacial division of the facial nerve which restrict the maneuverability of this division. The external carotid artery enters the compartment above the angulo-mastoid line and immediately gives rise to the posterior auricular artery. This vessel passes upward and backward on the periparotid fascial floor, making work along this plane more difficult. The superficial temporal and retromandibular veins are in close relationship to the facial nerve branches. These rami are found both superficial and deep to the veins. The external jugular is usually paralleled by an anastomotic branch between the transverse cervical and the cervical ramus of the facial nerve.

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IV

SURGICAL ALTERATIONS OF THE
LARYNGEAL LYMPHATICS

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An increasing awareness that carcinoma of the larynx may metastasize contralaterally as well as homolaterally in a significant number of cases has prompted the authors to review the lymphatic drainage of the larynx through the application of modern techniques. There have been several excellent clinical studies[3,4,7,9] relating the tendency to cervical metastases with the location of the primary lesion, though there are few articles[2,9] concerned with the problem of unexpected contralateral metastases.

In this report we have re-investigated the normal pathways of lymphatic drainage which comprise the control series and have further examined the alternate lymphatic channels which may be demonstrated by the eradication of the primary lymphatic pathways.

During the waning years of the nineteenth century and passing into the beginning decade of the current century, investigative interest aimed at clarifying the pathways concerned with laryngeal lymphatics was at its peak. These classical studies were confined to the normal larynx. The vital dyes (Prussian blue, Berlin blue, etc.) were employed for ease in visual observation and tissue analysis by the outstanding researchers, Rouviere,[11] Gerotta, Cuneo, Roubaud,[10] among others. Their efforts spanning almost a half century provided the basic hypothesis that the drainage occurred in a homolateral fash-

ion. Channels then proceeded from the hemilarynx to the correspond-
ing ipsilateral internal jugular nodes.

A few exceptions to the concept of homolaterality were recog-
nized and admitted. Quiret[8] reported a small series of experiments
in which he found that contralateral movement from a subglottic
site was inadequately defined in his report and for this reason the
impact of this important observation was diminished. Some years
later Quiret's experimental findings and conclusions were corroborated
by Rouviere[11] who established the possible existence of direct com-
munication between the lymph channels of one-half of the larynx
and the nodes of the opposite internal jugular chain.

In the intervening years from the basic anatomical research to
the current methods of therapy we have witnessed the utilization of
the radical neck dissection based on the sound principle of regional
nodal extirpation. The attack has been basically founded on the
concept of homolaterality of lymphatic activity.

The recent clinical reports of Jesberg,[2] Reed,[9] Ogura,[4] and Nor-
ris,[3] who found unexpected contralateral metastases from lesions,
well confined to the opposite hemilarynx, cast doubt on the univer-
sality of this classic opinion. In the two cases described by Jesberg,[2]
epidermoid carcinoma from a definitely unilateral tumor involving
the false cord and base of the epiglottis in the first case, and involv-
ing the periarytenoid area in the second, metastasized to the contra-
lateral cervical chain in fourteen and twenty-three months respec-
tively. In neither of these cases did ipsilateral metastases develop.
In the large series of cases reported by Reed,[9] 9% of the laryngeal
and hypopharyngeal neoplasms presented contralateral primary metas-
tases, though note was made that contralateral metastases were rare
from lesions within the lumen of the larynx. In the comprehensive
surgico-pathologic survey reported by Ogura,[4] we find reiteration of
that same point, that crossed metastases were not observed to originate
from the area which he designates as endolaryngeal. Crossed metas-
tases, however, were found in 10% of unilateral extrinsic and sub-
glottic carcinoma requiring secondary neck dissection on the remain-
ing side. In his critical analysis of surgical failures, Norris[3] reports
that 25% of thirty-two cases of unilateral carcinoma involving the
vestibular, marginal, or hypopharyngeal areas developed contralateral
metastases following simultaneous laryngectomy and neck dissection.

While these theoretically misdirected metastases are not the pri-
mary concern of the laryngologist, and do not suggest a radical depar-
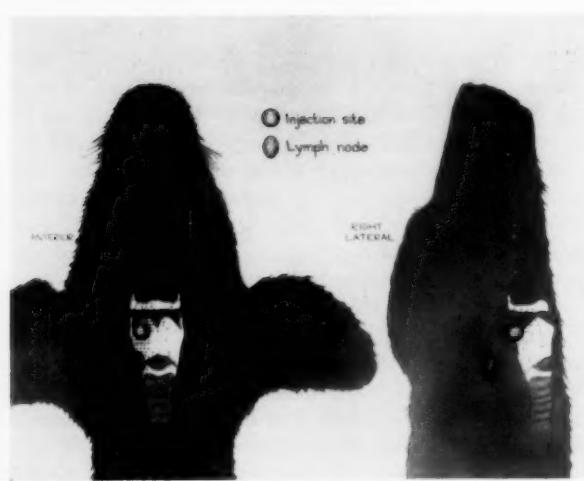
Fig. 1.—Scintigram demonstrating the movement of Au[198] from the supraglottic area to the homolateral suprapharyngeal lymph node in a normal dog.

ture from the currently accepted programs of therapy, nonetheless, they do occur with sufficient frequency to prompt this investigation.

It is our purpose to define in the laboratory situation these three areas of uncertainty:

1. What is the pathway and direction of lymph drainage in the normal test animal.

2. What pathophysiologic compensation takes place in the animal having been subjected to a unilateral cervical lymphadenectomy.

3. What is the duration of these alterations.

TECHNIQUE

Radioactive gold (Au[198]) prepared in the form of a stable cherry red colloid concentrate was selected to act as a tracer substance for several reasons. The radioactive particles, which are approximately 3 millimicrons in diameter, act as foreign bodies that are rapidly carried to the regional lymph nodes and phagocytized by the sub-

NORMAL *SUPRAGLOTTIC* INJECTION
NODAL GOLD
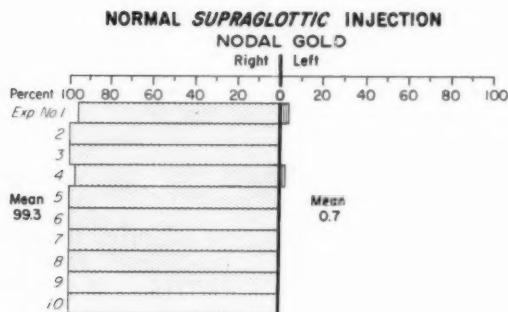
Fig. 2.—Distribution of nodal Au[198] from the right supraglottic area of the normal dogs.

NORMAL *CORDAL* INJECTION
NODAL GOLD
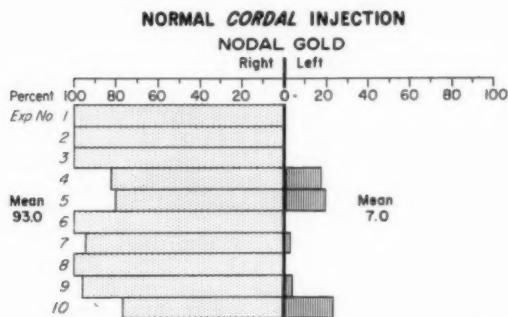
Fig. 3.—Distribution of the nodal Au[198] from the right cordal area of the normal dogs.

capsular reticulo-endothelial cells. Following injection, a blue hue immediately becomes apparent, thereby allowing a semi-accurate appraisal of the true site of injection. In tracer amounts, its radiation produces little tissue reaction. External scanning, using a scintiscanner* allows external detection of the lymphatic dynamics. Lastly, measuring the radiation emission in the well-type scintillation counter† provides quantitative measurements of endolaryngeal diffusion

* NRD Instrument Company, Model 31, St. Louis, Missouri.

† Nuclear Chicago, Model 132.

and lymphatic transport of the radiogold with a high degree of accuracy. These advantages supersede by far the limitations of the older methods of microscopic analysis.

The dog is ideally suited to the purposes of this experiment by virtue of the similarity in tissue mass and proportions to the human larynx. More importantly, there is only one node, i.e., the suprapharyngeal node, in each deep cervical chain responsible for collecting the lymph outflow from the larynx. In this sense, the common canine's neck may be looked upon as a larynx-lymph node preparation. While a few small nodes are found at the cephalic and caudal extremes of the cervical area, they are not related to laryngeal structures.

Of primary importance was the establishment of a volume which when injected would not diffuse beyond the midline of the hemilarynx. After many preliminary experiments to ascertain this optimal volume, 0.015 ml of the radiogold was observed to proceed in this fashion. As a result we can comment that in each experimental situation the submucosal instillation was a discrete unilateral deposit.

The colloid was measured and injected from a shielded tuberculin syringe fitted to a 23 gauge needle. The activity of this dilution ranged from 160 to 400 microcuries.

In the normal test animals, representing the control series, this small volume of test material was injected into one of the three laryngeal areas: supraglottic, cordal, or infraglottic. The fate of the substance was followed using both the scanning technique and postmortem fractional measurements of gold containing tissue. The second group of animals that had been previously subjected to a homolateral cervical lymphadenectomy was studied in the same fashion.

Under barbiturate anesthesia, the supraglottic and cordal areas were readily available for examination and precise injection employing the Jackson laryngoscope. The infraglottic area was less accessible so that a low tracheotomy with laryngoscopic illumination and visualization was found to be more satisfactory while not disturbing the important structures.

Forty-eight hours post injection the animals were sacrificed and a scintigram obtained in the frontal and lateral positions. The neck was then dissected, removing the larynx, the carotid sheath and their contents, and the neighboring soft tissue. In no instance was the

NORMAL *INFRAGLOTTIC* INJECTION

NODAL GOLD

Right | Left
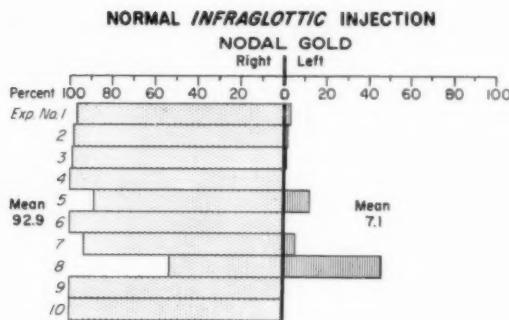
Fig. 4.—Distribution of the nodal Au[198] from the right infraglottic area of normal dogs.

tracer substance found in the liver or other remote areas of the animals. Pressman et al.[6] employing radioactive chronic phosphate observed a 20% loss via the excreta, though this observation was not made with radiogold. The larynx was divided vertically in the anterior and posterior midlines. The relative amount of the radioactive material in each hemilarynx and the suprapharyngeal nodes was measured in terms of percentage of the total recovered gold.

RESULTS

1. *Supraglottic Area.* The site of injection in the supraglottic area is in the false cord midway between the anterior midline and arytenoid cartilage. During the introduction of the dye, pigmentation is observed to dissect subepithelially outlining a triangular shaped area with the apex directed anteriorly. After 48 hours, the animals were sacrificed and the scan (Fig. 1) which was taken showed a well defined area of radioactivity posteriorly and laterally to the injection site. This movement is not striking when the scan is taken in the anterior-posterior direction because of the proximity of the gold containing structures in that plane, but is immediately apparent on the lateral scan. The necks were then dissected for fractional analysis of the gold containing structures and it was found that approximately 50% of the gold had migrated to the suprapharyngeal nodes.

Figure 2 shows the results of ten dogs analyzed in this fashion. The vertical bold line beneath the 0% mark represents the midline.

SUPRAGLOTTIC INJECTION *AFTER* NECK DISSECTION

NODAL GOLD

Right | Left
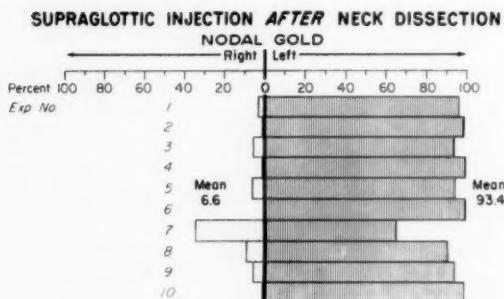
Fig. 5.—Distribution of the nodal Au[198] from the right supraglottic area of the dogs subjected to a right cervical lymphadenectomy.

The bars on the right side represent that amount of the total nodal gold which has collected in the right suprapharyngeal node. The bars on the left represent that fraction of the extra laryngeal test substance moving to the left suprapharyngeal node.

Lymphatic drainage from the right supraglottic area is seen to be purely a unilateral phenomenon in eight of the ten test animals, while the remaining two show 5 and 2% movement to the contralateral deep jugular chain. The mean homolateral movement from the supraglottic area is 99.3% while the mean contralateral movement is 0.7%.

2. *Cordal Area.* The injection into the true cord was accomplished with more difficulty than in the other area. The needle was introduced half way between the anterior commissure and the base of the arytenoid. In the majority of cases, the dye could be seen distending the epithelium overlying Reinke's space, though in a few instances the injection was made into the vocalis muscle. The scintigram of the radioactivity is identical with that of the supraglottic area except that the depot site was more caudad; corresponding to the location of the true cord.

Figure 3 shows the relative movement of the radiogold to each of the deep cervical chains in this group of ten animals. Half of these animals show a decidedly unilateral lymphatic outflow while the remaining five show bilaterality of drainage. In these last five experiments the percentage of extralaryngeal gold in the left suprapharyngeal node ranged from 3.0 to 26.0% respectively.
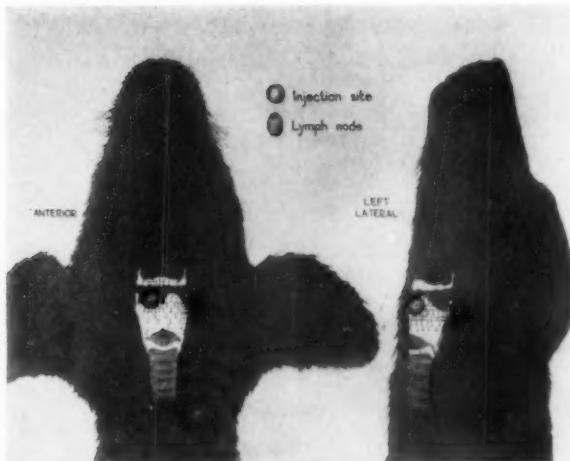
Fig. 6.—Scintigram demonstrating the contralateral movement of Au[198] from the right supraglottic area of a dog subjected to a right cervical lymphadenectomy.

3. *Infraglottic Area.* The tracer material was introduced via a low tracheotomy incision into the infraglottic tissue approximately eight millimeters posterior to the anterior commissure. This point is half way between the anterior commissure and the base of arytenoid in the majority of mature dogs. The configuration of the depot site in this area was roughly circular or rectangular, corresponding to the shape of the subglottic area. The scintigram of the extralaryngeal movement of the radiogold was essentially the same as that of the supraglottic area.

This graph (Fig. 4) shows that lymphatic drainage from the infraglottic area is predominantly a homolateral occurrence, while more variability in the pattern is observed. Six animals had bilateral drainage, though the amount moving to the left was small in each case except experiment number eight. The range of movement to the contralateral node was 1.7 to 46.8%. The mean movement to the right in this series of ten animals was 92.9%. The mean movement to the left was 7.1%.

The second phase of this investigation is concerned with the pathophysiologic response of the dog to an induced unilateral lymph-
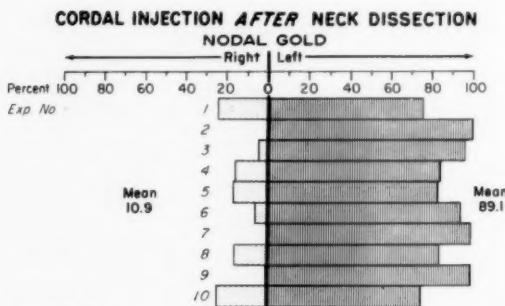
Fig. 7.—Distribution of the nodal Au[198] from the right cordal area of the dogs subjected to a right cervical lymphadenectomy.
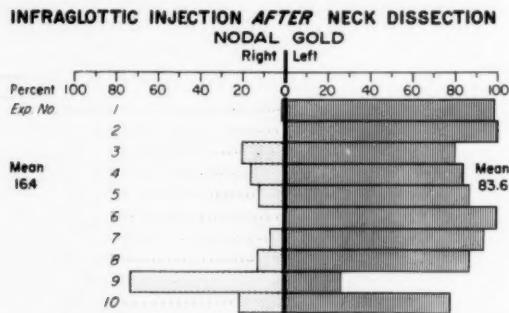
Fig. 8.—Distribution of the nodal Au[198] from the right infraglottic area of dogs subjected to a right cervical lymphadenectomy.

atic obstruction. This condition was attained by the most certain method available, i.e., surgical extirpation of the right carotid sheath and its contents, sparing the carotid arteries and the vagus nerve. After a convalescent period of six weeks, the right hemilarynx was injected with the radiogold and the lymphatic outflow from the supraglottic, cordal, and infraglottic areas followed by the same techniques as employed in the series of normal animals.

RESULTS

1. *Supraglottic Area.* Figure 5 shows the change in lymphatic flow which has been induced by a right cervical lymphadenectomy.

LYMPHATIC DRAINAGE *16 WEEKS* AFTER NECK DISSECTION
NODAL GOLD
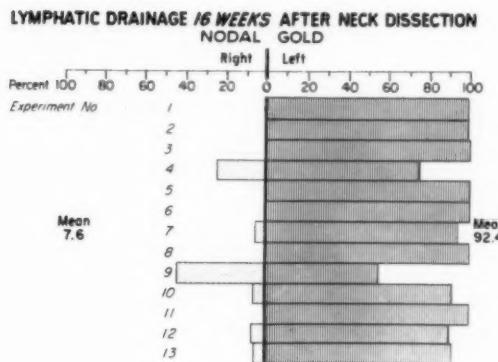
Fig. 9.—Distribution of the extralaryngeal Au[198] in the suprapharyn-
geal nodes of dogs subjected to a right cervical lymphadenectomy sixteen
weeks prior to this analysis.

Lymph flow as determined by this fractional study of the gold bear-
ing tissue has been reversed and drains to the contralateral deep cervi-
cal chain. The contralateral outflow is predominant in all animals;
it is exclusively contralateral in four; and bilateral in six with the
movement to the right ranging from 0 to 34.6%.

The mean movement to the left is 93.4% and to the right is
6.6%.

The scan taken of the neck (Fig. 6) shows unequivocal move-
ment of radiogold to the left suprapharyngeal node.

2. *Cordal Area.* The direction of lymphatic flow from the right
vocal cord in those animals devoid of the regional nodes is again to
the left suprapharyngeal node. Figure 7 shows mean movement to
the left jugular node of 80.1% and homolateral movement of 10.9%.
The range of homolateral drainage was 0 to 25.0%.

3. *Infraglottic Area.* This bar graph (Fig. 8) again demon-
strates the same observation that lymphatic drainage from the larynx
deprived of the regional nodes is primarily a contralateral occurrence.
The mean movement to the left is 83.6% and to the right 16.4%.
The range of movement to the right is 0 to 67.6%.

The third and last part of this study was designed to determine the duration of this deviation in lymphatic outflow incurred by a unilateral cervical lymphadenectomy. Thirteen animals were subjected to the surgical procedure and were similarly tested after a period of sixteen weeks (Fig. 9). No significant change in this induced variation was noted in this group as compared to those animals tested six weeks after the lymphadenectomy. The bar graph illustrates the findings in a series of thirteen animals. The mean homolateral movement of the radiogold was 7.6% in this series.

CONCLUSIONS

As a result of the research carried out on the canine larynx, the following conclusions can be drawn:

1. A technique employing radiogold has been described to determine the lymphatic outflow from the larynx in qualitative and quantitative terms.

2. Lymphatic outflow from the three major areas of the normal larynx is predominantly a homolateral event. In this series exclusively unilateral drainage occurred in 56.7% of the animals while the remaining 43.3% manifested bilaterality of drainage. The range of contralateral movement of the gold was 0 to 46.8% with a mean of 4.4%.

3. Surgical extirpation of the regional node produces a condition of lymphatic obstruction characterized by contralateral lymphatic drainage from each of the test sites. Thirty per cent of the animals manifested only contralateral lymph flow. The remaining 70% demonstrated predominantly contralateral drainage with a lesser amount of the test material moving to the previously operated site. The range of homolateral movement in this series was 0 to 67.6% with a mean of 11.3%.

4. There was no evidence of lymphatic regrowth in those animals examined by this technique sixteen weeks after the performance of a cervical lymphadenectomy.

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V

TISSUE REACTION FOLLOWING RECONSTRUCTION
OF THE OVAL WINDOW
IN EXPERIMENTAL ANIMALS

III.   OSSICULAR REPLACEMENT OF STAPES

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As previously outlined,[1] three main experiments have been under-taken in an effort to construct a mobile sound-transmitting cover for the oval window in cats, following stapedectomy.   Presentation of the method and results has been grouped in three parts.   Parts I and II dealt with the use of vein graft, polyethylene tubing and gelfoam. These data were presented at the American Otological Society in March, 1960.

Part III of this series of experiments is herewith presented. These procedures deal with replacement of the stapes by ossicular trans-plants.   It had been previously demonstrated by us that a stapes could be surgically removed from the oval window and from its stapedioincudal articulation, then immediately and successfully re-aligned.[2,3]   These results suggested to us that it might be feasible to replace the stapes with transplants.   We had shown that the stapes, removed and immediately replaced, exhibited connective tissue adher-ence to the walls of the oval window, three days following operation. In spite of the fact that a replaced autogenous stapes became anky-losed four and one-half months postoperatively, we felt our results warranted further investigation along these lines.

The critical problem lay in the possibility that the tissue of the oval window might reject a foreign ossicle, or if it were accepted,

that the ossicle might become ankylosed as did the replaced autogenous stapes. Experiments employing 9 cats and 10 ears were performed to attempt to throw light on these problems. The animals were permitted to live from 6 days to 11 months after the surgery.

The following procedures were carried out:

Procedure 1. Replacement of a cat stapes by a fresh sibling stapes. Cat #22, Right ear. Autopsy #302; postoperative time, 11 months.

Procedure 2. Replacement of a stapes by fresh homologous stapes (not sibling).

Cat #21 Left ear. Autopsy #211; postoperative time, 6 days.

Cat #28 Left ear. Autopsy #235; postoperative time, 7 weeks.

Cat #30 Right ear. Autopsy #306; postoperative time, 4 months.

Procedure 3. Replacement of a stapes by bank stapes.

Cat #33 Right ear. Autopsy #283, postoperative time, 6 days.

Cat #31 Right ear. Autopsy #262, postoperative time, 16 days.

Cat #32 Right ear. Autopsy #277, postoperative time, 5 weeks.

Cat #23 Right ear. Autopsy #346, postoperative time, 2 months.

Procedure 4. Replacement of a stapes by autogenous incus.

Cat #23 Left ear. Autopsy #346; postoperative time, 11 months.

Procedure 5. Replacement of a stapes by a fresh incus from another cat.

Cat #24. Autopsy #246; postoperative time, 3½ months.

OBSERVATIONS

The contour of the stapes in the cat is quite different from that of the human ossicle.[5,6] There is no well-marked differentiation between anterior and posterior crus, such as is usually present in the human stapes. In the human ear the posterior crus is commonly more bowed than the anterior.[7] Occasionally, however, in the human ear, situs reversus may occur, so that the anterior crus is the more bowed. In the cat, as illustrated in Figure 1, both crura are relatively straight. A survey of the stapedes of lower mammals reveals that in Rhesus monkey and even in rodents such as guinea pigs which possess
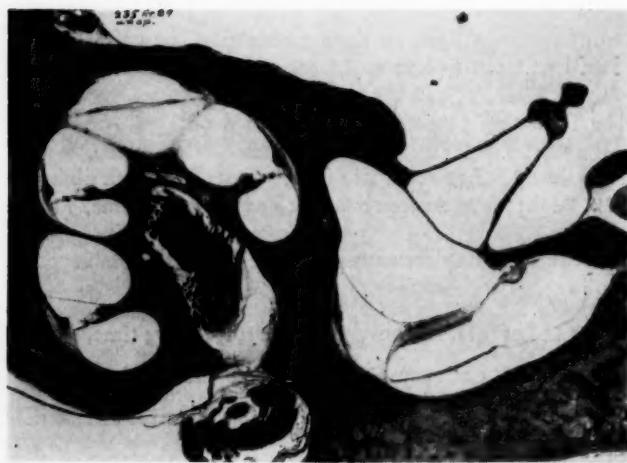
Fig. 1.—Normal right unoperated stapes of the cat. Note that the crura in this animal are relatively long in proportion to the footplate and that they are not bowed. There is no appreciable difference between anterior and posterior crus, as in the human stapes. No. 235, section 89.

Fig. 2.—Stapedial transplant from a sibling. The foreign stapes is not quite perfectly fitted into oval window but it is clear that it is viable. Posteriorly it is attached to the vestibular wall by fibrous tissue, anteriorly, by bone. No. 302 right, section 100. Postoperative time 11 mos.
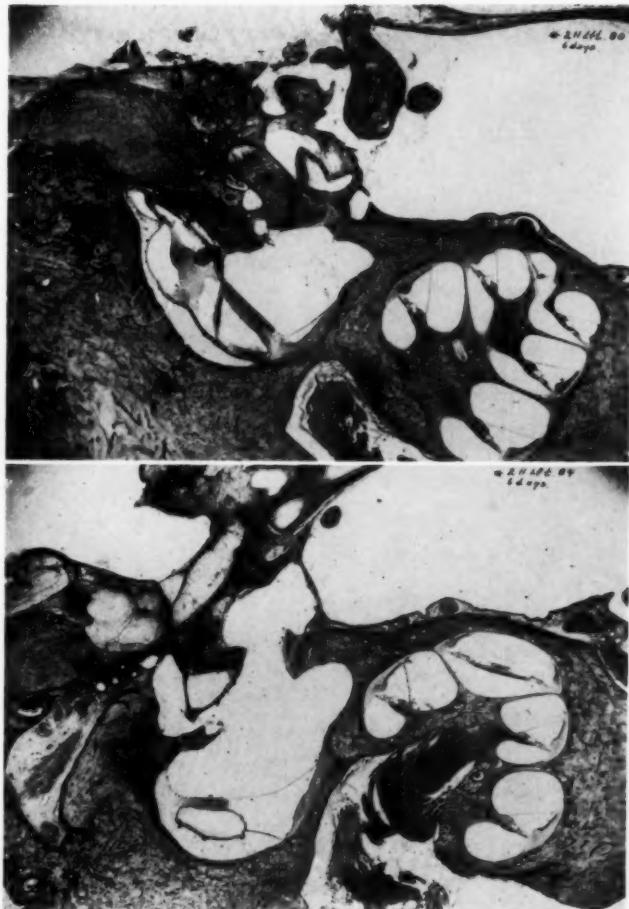
Fig. 3.—In spite of extensive displacement of this homologous trans-plant as seen in lower photo where a fragment of autogenous stapes remains, the delicate endosteal membrane shown in the upper level was sufficient to protect the inner ear. No. 211 left, sections 80 and 84. Postoperative, 6 days.
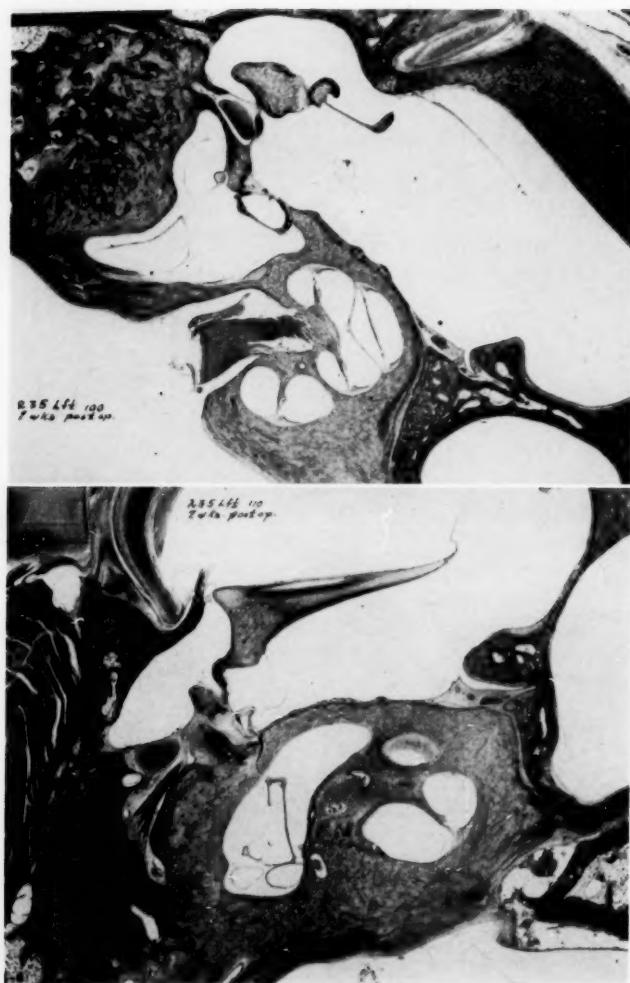
Fig. 4.—Stapes removed from oval window inadvertently fell into vesti-
bule. No tissue reaction to its presence followed during 7 weeks postopera-
tive period. A fresh stapes from another cat was inserted into the window.
This was fractured but healed, proving it to be viable. See Figure 6, left,
sections 100 and 120.
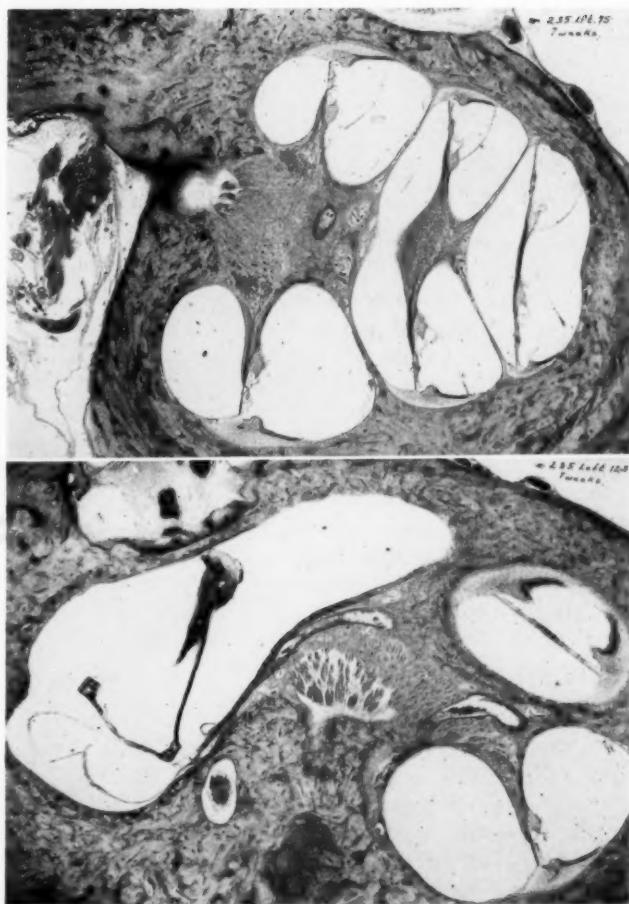
Fig. 5.—The upper photo shows membrana vestibularis (Reissner's) in situ throughout. It is slightly bowed outward, indicating excess pressure within the endolymphatic system. This fact is further demonstrated in the lower photo where ductus reuniens exhibits distension and the footplate of the autogenous stapes rests on the outer wall of the utricle. The endolymph apparently buoyed the stapes sufficiently to prevent tearing the membranous labyrinth. No. 235, sections 75 and 123. Postop. time, 7 weeks.

a persistent stapedial artery, the posterior crus is not more bowed than the anterior.   This is true in spite of the fact that the stapedius muscle is proportionately larger in the lower animals than in the human ear.

A further difference in the shape of the ossicle may be observed in the footplate.   The human stapes is "bean-shaped."   The cat's footplate is almond-shaped, one end (posterior) being only slightly more pointed than the other.

The crura of the stapes in the cat possess the hollow beam structure or open trough contour which occurs in the human stapes.[6]   This was rarely observed by us in the sections of the cat's ear, because of the fragility of the ossicle and the fact that we rarely stained every single section in the cat series.   The upper photograph of Figure 3 reveals the curved contour at the base of the crus.

Procedure 1.   The right stapes of kitten #22 was removed and replaced by the fresh left stapes of a sibling kitten.   Operative notes stated that the implanted stapes was well-set but that the rim did not fit perfectly.   Eight days following the operation a notation stated that the kitten was in excellent playful condition.   Six months following this operation a vein graft was done on the opposite ear.   Nine months following the first operation the cat was playful and jumped from a chair readily.   Response to sound was present.   At the end of eleven months the cat was sacrificed.

Figure 2 shows that this stapes is in situ but that it has ankylosed anteriorly.   There is incipient ankylosis posteriorly (Cat #22, Autopsy #302).   The fact that the head of the stapes is not seen in the illustration does not mean that it has been resorbed by the connective tissue present.   It simply means that the knife was not cutting in the perfect plane of the crura and head.   The head appears in previous sections, and like this portion of the stapes is viable.   The head is attached to the incus by fibrous tissue.   Thus the continuity of the ossicular chain was re-established.   Inner ear is in good condition 11 months after the operation, except for inner sulcus cells of the basal turn which have sloughed in a continuous band from their attachment.   The hearing which this cat possessed at the time of death was probably from the other ear, however.

Procedure 2.   Cat #21, Autopsy #211.   A fresh stapes from a cat, not a sibling, was used to replace an autogenous stapes.   In removing the autogenous stapes the crura were fractured and the
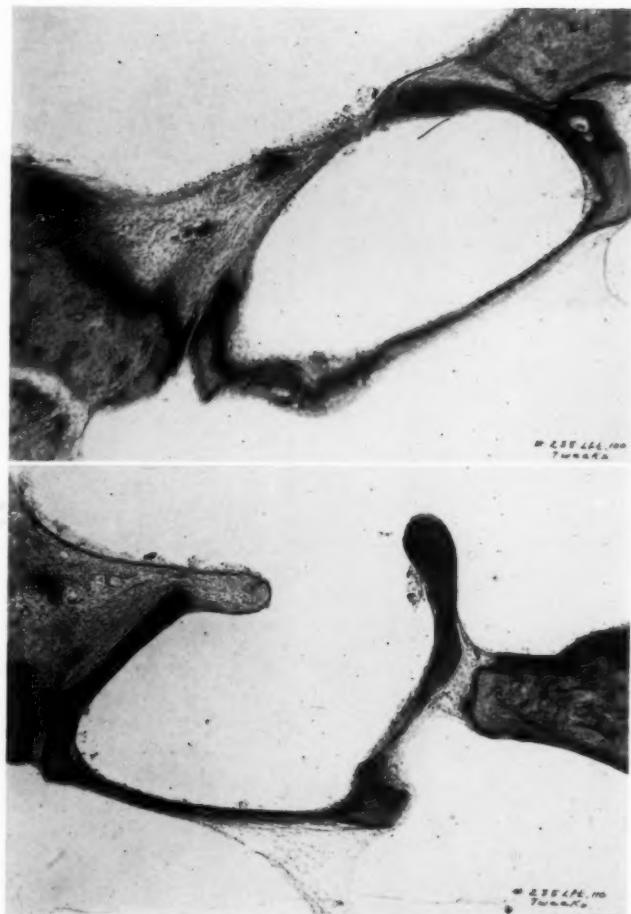
Fig. 6.—Details of inserted kitten stapes showing viable state of this homogenous graft. Repair of the anterior fractured crus and callus formation on the partially fractured footplate have occurred. Incipient ankylosis is present. No. 235 left. Postop., 7 wks.
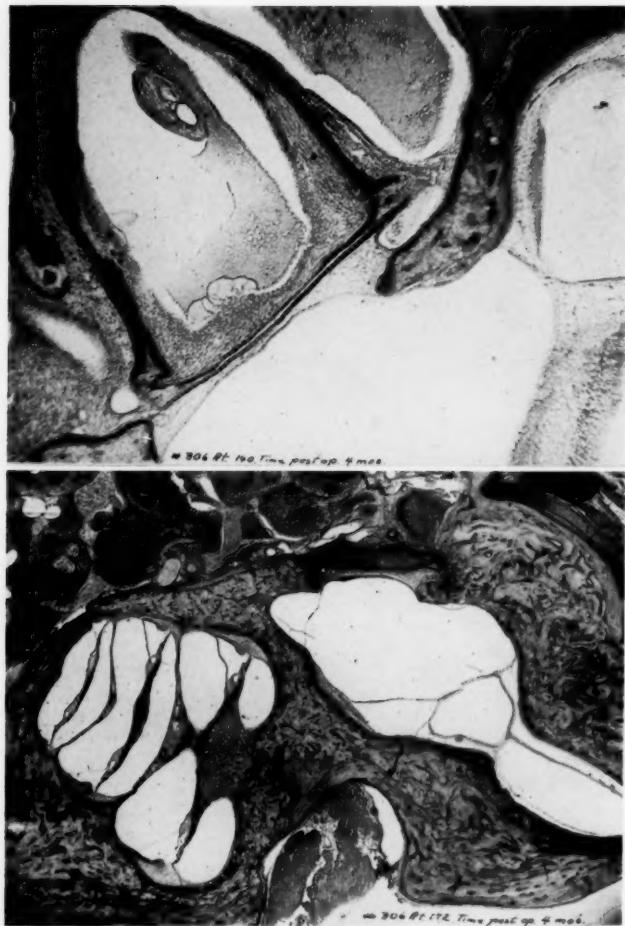
Fig. 7.—Right stapes removed and replaced by fresh right stapes from cat No. 31. Transplant appears slightly larger than oval window. The endosteal membrane which formed has, thus far, protected inner ear from otitis media. At the lower level a fragment of the autogenous stapes remains in situ, posteriorly. Anteriorly the implant has become heavily ankylosed. Time postoperative, 4 months. No. 306 right, sections 140 and 172.
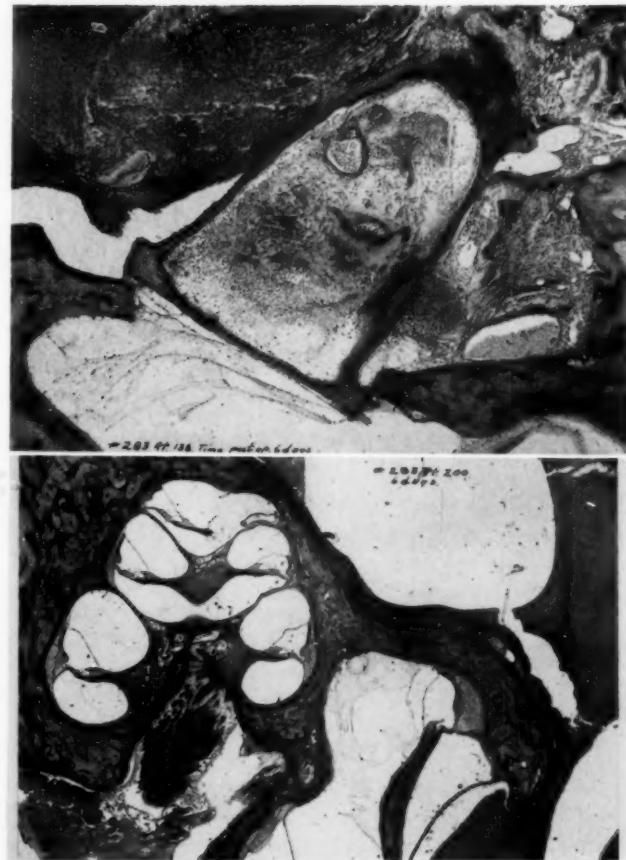
Fig. 8.—Bank stapes, in situ, 6 days. Although it is attached by connective tissue to the oval window, anchorage was not sufficiently firm to prevent middle ear infection from invading inner ear. No. 283 right, sections 136 and 200.

footplate was accidentally displaced into oval window. This was painstakingly picked out before positioning the homologous transplant. Operative notes stated that the facial nerve was forcibly retracted; also the incus. "The transplant was beautifully placed." Immediately following the operation the animal exhibited a weaving, swaying movement of the body. Four days after the operation the animal appeared to be in excellent condition and ate heartily but it died on the sixth day. Figure 3 shows that the transplant remained in position superiorly and that a delicate membrane had closed the oval window beneath the footplate. But the view of the lower level (84) reveals that a fragment of the autogenous stapes remained at the stapediovestibular joint, the homologous stapes is dislodged and no endosteal membrane covers this level of the oval window. Nevertheless the membrane present on the upper level appears to have been sufficient to protect the inner ear up to the time of death. Reissner's membrane is in situ. Organ of Corti is in good condition except for necrotic nuclei. These are to be expected in an animal which had died over the week-end and was not perfused. Autopsy revealed a ruptured intestine and peritonitis as the probable cause of death.

The second cat in Procedure 2 was cat #28, autopsy #235. Operative notes state that in this cat the whole left stapes was inadvertently pushed into the vesibule and the surgeon could not hook it out. Nevertheless the stapes from a kitten was placed in the oval window. This cat was able to play with a paper ball a month following the operation. It walked and ran well but sometimes held head slightly to the left. The opposite ear was never operated. Seven weeks after operation the animal became sick and was sacrificed. Impaction of the rectum was found and undoubtedly was the cause of death.

Figures 4, 5 and 6 illustrate the interesting results in this animal. The upper photograph, Figure 4, shows that the implant was a little too small for this oval window and became subluxated. The lower photograph reveals the stapes which was displaced into the vestibule to be gently poised on the lower wall of the utricle. It does not, in any section, appear to exert sufficient pressure on this wall to alter the shape of the utricle. Evidence that some pressure was exerted, however, is seen in the fact that Reissner's membrane is bowed outward in every coil of the cochlea (section 75), and that the ductus reuniens is unusually prominent and distended as shown in section 123.

Figure 6 demonstrates the viable state of the implanted homologous kitten stapes. The surgeon noted that the anterior crus was
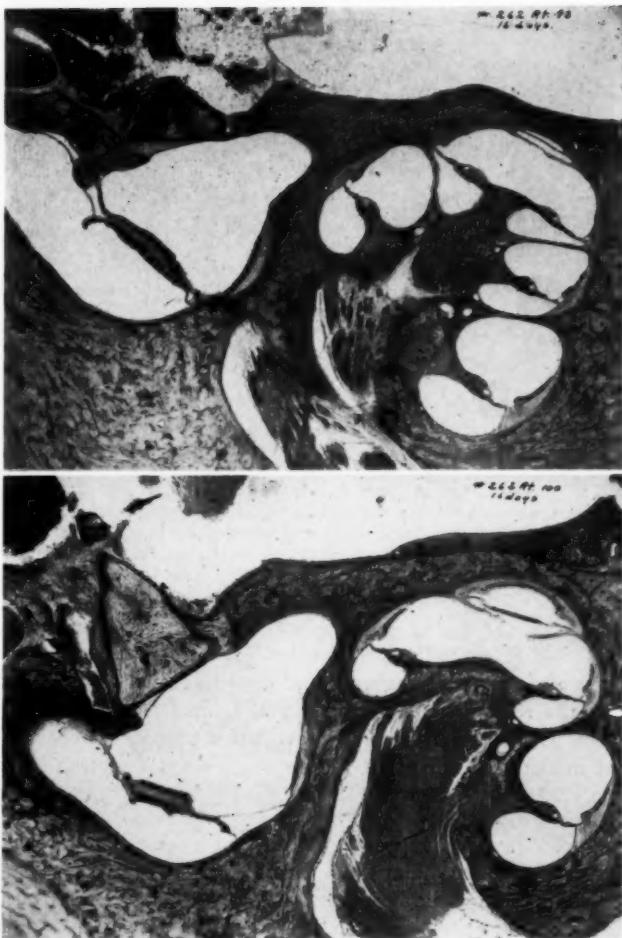
Fig. 9.—(A) Bank stapes in situ, 16 days postoperative. An endosteal membrane covers oval window. Inner ear is thus protected from the purulent otitis media. Trauma to the inner ear, probably at stapedectomy, has ruptured the outer wall of saccule with consequent collapse of the entire endolymphatic system. No. 262, section 90, right.

(B) The otitis media is obviously being resolved at this level. Had damage not occurred to the inner ear, this would probably have been a successful result. No. 262 right, section 100.

Fig. 10.—Autogenous incus articulated with malleus and fitted fairly well into oval window. An early otitis media has appeared. The opposite ear was heavily infected; otitis media and labyrinthitis being present. Inner ear on this side has thus far been protected by the presence of the incus in the oval window. No. 346 left, sec. 90. Postop. time, 11 mos.

inadvertently fractured in the transfer. It is apparent that the foot-plate was also partially fractured and a well-formed callus has developed in the seven weeks postoperative. Thus it is clear that this transplant is sufficiently viable to institute a process of repair. As is evident in the lower photo of Figure 6, incipient ankylosis is present posteriorly.

Figure 7 reveals the protective effect of a fresh homograft in the presence of an otitis media but unfortunately the stapes is firmly ankylosed inferiorly as indicated by the heavy black deposit of calcium at the anterior stapediovestibular junction. Postoperative time was four months (Cat #30, Aut. #306).

It is worthy of note that the tendon of the stapedius muscle has held its replaced position at the head of the transplanted stapes, in spite of the heavy infection in the middle ear. This condition could not be photographed but knowledge was gained by painstakingly reading serial sections. The stapedius muscle appears viable but actual movement of the stapes would have been gradually curtailed with the developing ankylosis illustrated in the lower photograph.
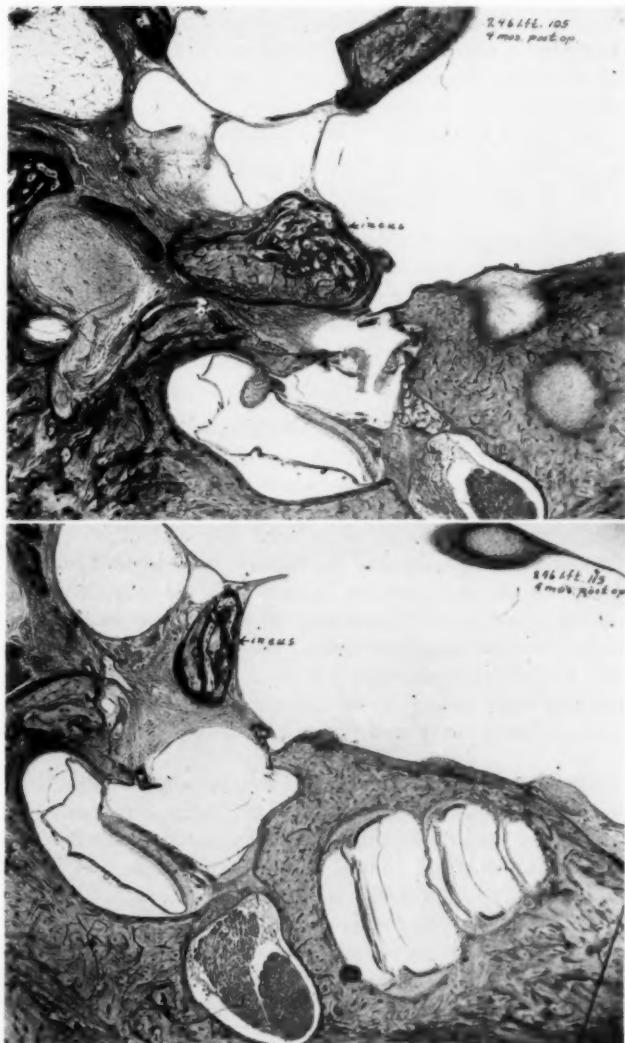
Fig. 11.—Stapes removed except for fragments at each end of oval window as seen in lower section. Fresh incus from another cat was placed in oval window. Fibrous tissue has closed window but foreign incus has become dislodged and is undergoing osteomyelitis. No. 246 left, sections 105 and 115. Postoperative time, 4 months.

We now turn to the use of the bank stapedes. These ossicles, upon removal, were placed in a dry sterile dish, covered and taken to the refrigerator used for bone bank surgery transplants, for human plastic surgery in this hospital. The temperature maintained is 10° C. Ossicles were used from several days to weeks or months later. The first stapes remained in situ 6 days before sacrifice of the cat. The ossicle was found connected to the vestibular wall by delicate fibrous bands but these were not enough to prevent labyrinthitis setting in as a result of otitis media (Fig. 8).

Figure 9, on the other hand, illustrates a bank stapes which was in situ 16 days. It was well-placed on an endosteal membrane and the inner ear was protected from an otitis media. But evidently the outer wall of the saccule was inadvertently damaged at surgery and this is reflected in the collapse of the endolymphatic system throughout the inner ear.

Bank homologous stapedes from cats #32 and #23, autopsy #277 and #346, respectively, gave unsatisfactory results, having been left in situ for periods of five weeks and two months respectively. Both animals developed purulent labyrinthitis.

Procedure 4 is illustrated in Figure 10. An autogenous incus was placed in the oval window from which the stapes had been removed. As shown in the illustration it was aligned with the malleus to which it became ankylosed during the eleven months postoperative period. An endosteal membrane formed which was sufficient to protect the inner ear up to this time, from the otitis media present. The opposite ear had a heavy middle ear infection and labyrinthitis.

Procedure 5 consisted of using a homologous incus as the transplant. This incus, although not too perfectly fitted into the oval window at the time of death, was well anchored in the oval window with dense fibrous tissue. There is no evidence of an otitis media but part of the foreign incus exhibits osteomyelitic change. Whether this condition arose from the reaction to the host or whether it arose from a middle ear infection, resolved before the time of death, cannot now be stated.

SUMMARY AND CONCLUSIONS

From the clinical point of view these cats appeared to suffer less discomfort following this type of procedure than from the many others to which we subjected some of them. We had only two in this group, #346 left and #211 left, which exhibited swaying and

weaving movements, following surgery. Most of the cats recovered more promptly and were playful earlier than in the other types of operations.[1-4]

The microscopic observations, on the other hand, do not yield particularly hopeful results. In the one case in which the stapes was held in place by gelfoam (#346 right) the stapes did not remain in situ and the inner ear exhibited the same type of labyrinthitis, fibrosis and new bone formation described in previous reports on the use of gelfoam.

We do find it highly informing to know that in the cat a homologous stapes will not only "take" but will repair itself in the host environment, thus proving its viable state.*

We believe that where ankylosis occurred some injury to the bone was inadvertently produced and this reaction was response to injury and effort to repair.

We feel encouraged again at the amount of manipulation the inner ear will tolerate and have again demonstrated (Fig. 9, #262 right ear) the devastating effect that damage to the outer wall of the saccule can cause. Observations of the buoyancy of the perilymph and the tolerance of the presence of the whole stapes within the vestibule for a period of 7 weeks are surprising. Of course, we are dealing with a four-footed animal in this experiment. It would be interesting to try inserting a columella in a two-footed animal like the bird to see if equilibrium would be more difficult to maintain.

We find it encouraging to think that a stapedial tendon can be made to adhere to a foreign stapes, even in the presence of a suppurative process. Its function, however, would certainly have been curtailed as the ankylosis developed.

These animals were not given antibiotics unless they showed signs of a cold or similar symptoms. In the future it might be helpful to forestall the otitis media and viral infections by their use. Knowledge is gained, however, by observing that these procedures provide a barrier to middle ear infection and prevent its invasion of the inner ear in many instances.

210 E. 64TH ST.

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* Heterologous ossicles (that is, ossicles from other species) have not been included in our procedures.

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VI

CAPILLARY PERMEABILITY
OF THE COCHLEA

AN EXPERIMENTAL STUDY

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It has been considered that increased permeability of the blood vessels of the inner ear may play a causative role in Ménière's disease or endolymphatic hydrops. Even if disturbances in capillary permeability do not produce endolymphatic hydrops, slight changes in composition of the endo- and the perilymph may lead to the development of inner ear disease.

Apart from pathological conditions, production of the endo- and the perilymph are intimately related to the permeability of the vessels supplying the organ responsible for the formation of the fluids.

Permeability is one of the important functions of the blood vessels. Blood-borne materials and metabolites penetrate the wall of the vessels from the blood stream into the tissues, and there may be difference in various parts of the blood vessels even in the same organ.

Under particular experimental conditions, permeability has also been used to mean extravascular leakage of foreign substances such as dye-stuffs that have been injected into the circulation. In 1885 Ehrlich found that intravenous injection of vital dye Coerulein-S promptly stained most organs, but left the brain unstained. Since then, many investigators have endeavored to elucidate this problem.

To explain this phenomenon it has been postulated that there must exist a "barrier" between the brain and the blood that prevents noxious substance in the blood stream from invading the brain substance. As the term "barrier" is apt to be interpreted as an absolute prohibition against penetration, "potential-barrier" has occasionally

been used to express a potential gradient that must be overcome
before a certain process can occur (Davson[1]).

Though there exist barriers in various tissues, the restriction to
passage of matter from blood to brain is peculiar, therefore, studies
have been made mainly on blood-brain barrier. As yet the site and
the mechanism that regulates the transport of matter from blood to
brain has not been determined. When we reflect upon the problems
in the inner ear, it may be said that the inner ear, like the brain, is
hardly stained by vital staining.

Several ways such as dye studies, microquantitative studies and
radio-isotope studies are experimentally available for investigation
of the barrier problem, but in practice their applications to the inner
ear are comparatively difficult chiefly because of the tiny size of the
organ. To observe the permeability characteristics of the inner ear
vessels, vital dye staining of the animals seems to be an expedient
method.

The present report is designed to provide information about the
relation of dye passage to the blood vessels of the inner ear.

METHOD

In the experiments, adult albino guinea pigs weighing about 350
grams were used. They were anesthetized with intraperitoneal admin-
istration of 25% urethan solution and then tracheotomized. The
cochleae were approached through the bulla tympanica from the ven-
tral aspect. After removal of the mucous membrane, which covered
the cochlea and the internal surface of the bulla tympanica, a fenestra
was made with a fine probe at the apical end or the third coil of the
cochlea by removing a small part of the bony wall. This was done
under the binocular microscope (Zeiss-Otoskop).

Using the especially designed microscope, small vessels of the
spiral ligament and the stria vascularis could be clearly observed
through the fenestra. Simultaneously the blood pressure was directly
measured in one side of the carotid artery and a record of the breath-
ing was made on smoked paper.

Vital staining was performed by the intracardial injection of
5 to 10 cc of 1% trypan blue solution (small amounts of histamin
or ethyl alcohol-acetic acid solution added). Congo red and India
ink solution were sometimes used as substitutes for trypan blue solu-

A   B
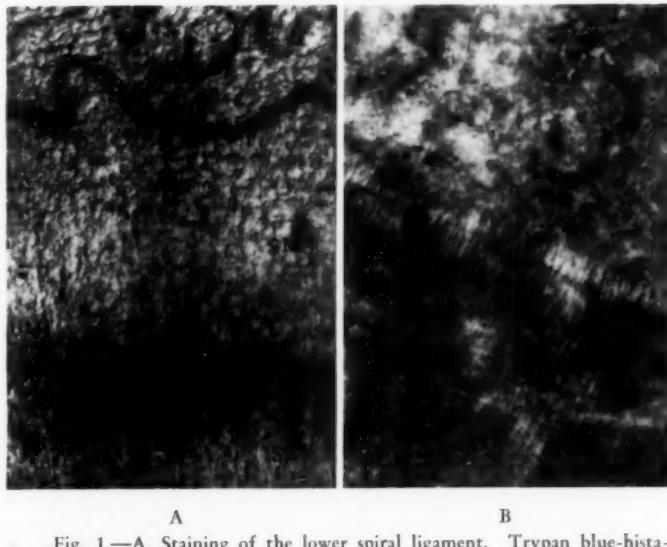
Fig. 1.—A. Staining of the lower spiral ligament. Trypan blue-hista-
mine injection. X 400. B. India ink-histamine injection. X 400.

CAP, strial capillary. SM, wall of the scala media. STY, wall of the
scala tympani. BM, attachment part of the basilar membrane.

tion. Observations were made on the exposed area of the spiral liga-
ment and the stria vascularis or the perilymphatic space of the scala
tympani of the basal coil through the round window membrane.

After the dye had entered the small vessels of the area, the spiral
ligament and the stria vascularis were taken out. Great care was taken
to avoid excessive damage to the tissues which were thoroughly exam-
ined under the microscope at magnifications of 40 x to 400 x for
extravascular leakage of the dye.

The brain, kidney and the remainder of the inner ear were
rapidly fixed in formalin. Paraffin sections of these tissues were
examined.

RESULTS

The following experimental results were obtained from the re-
moved spiral ligament.
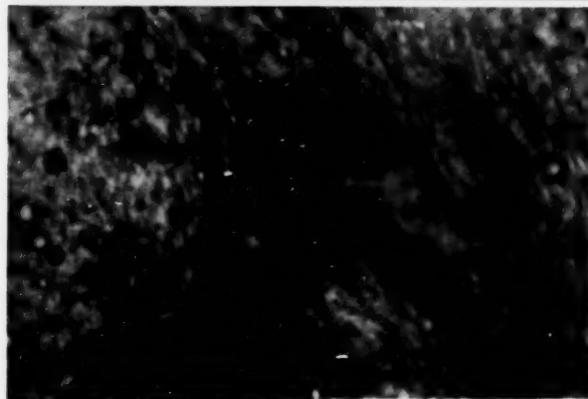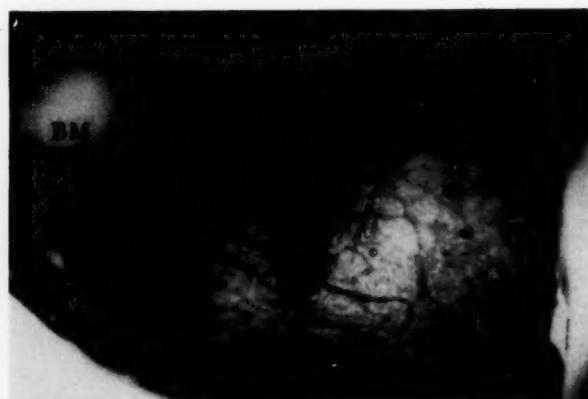
Scala Tympani. The lower spiral ligament which formed the lateral wall of the scala tympani was clearly stained, though degrees of coloring were variable. The staining was so distinct that one could easily detect the coloring macroscopically. With congo red and India ink the same results were obtained.

The coloring was definitely bordered by the attachment of the basilar membrane and within the part of the scala media no trypan blue was detectable (Fig. 1A, 1B). The farther from the line basalwards, the weaker the coloring. This finding was observed through all of the spiral ligament from the basal coil to the apex, but it did not show the relation of dye and the vessels from preparations of the second, the third and the apical coil. However, a preparation obtained from the basal coil revealed that trypan blue was deposited immediately adjacent to the wall of the venules (Fig. 2). Furthermore, when an intravitam microscopical observation on the perilymphatic space of the scala tympani of the basal coil was made through the round window membrane, trypan blue was noted to pass into the lumen.

It is evident from these findings that trypan blue permeated the wall of the venules in the lower spiral ligament and passed rapidly into the perilymph of scala tympani during the survival of the animal. The lower spiral ligament of the basal coil was easily stained.

Scala Vestibuli. Unlike the findings of the lower spiral ligament, coloring of the upper spiral ligament was usually not observed, though sometimes stained nuclei of the endothelial cells were found.

It was sometimes observed that faint diffuse coloring was detectable around the vessels where the radiating arterioles or precapillary vessels branched off, but not peripheral from them (Figs. 3, 4). It was uncertain whether small amounts of dye which leaked from the vessels intermingled with the perilymph of the scala vestibuli.

Scala Media. Staining the lateral wall of the scala media was usually not observed, though in rare instances faint and speckled

Fig. 2.—Extravascular leakage of trypan blue along the wall of the venule in the basal coil. BM, Basilar membrane attached here. X 90

Fig. 3.—Dye escape from the bifurcation of the precapillary in the upper spiral ligament. X 400

Fig. 4.—Enlargement of Figure 3. X 400
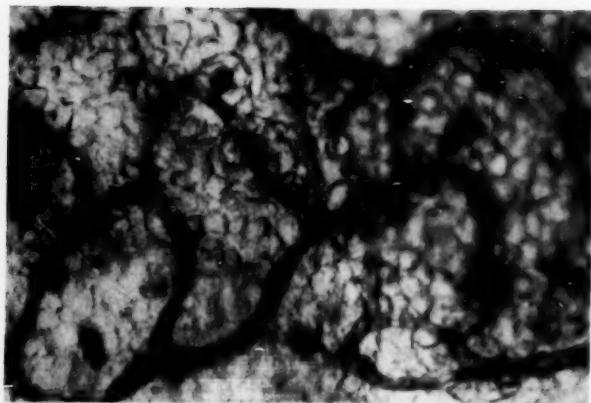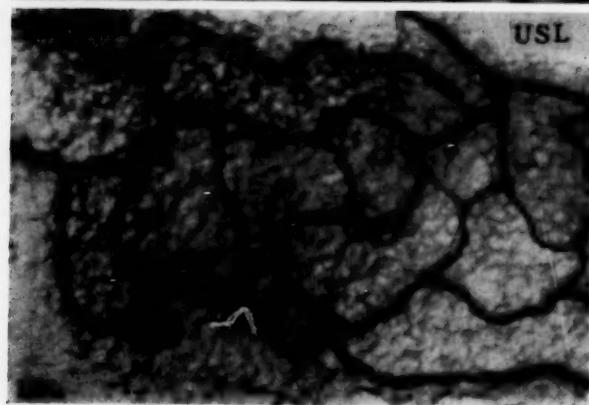
staining around the vessels was observable between the stria vascularis and attachment of the basilar membrane. In the thicker part, however, the lower part of the median spiral ligament was faintly stained.

In the stria vascularis no matter how full the capillaries were with trypan blue, extravascular leakage of the dye was never seen microscopically. It is remarkable that cells which took the dye were scattered over the stria vascularis in the vicinity of the capillaries (Figs. 5, 6).

The attachment of the stained cells to the wall of the strial capillaries, probably indicated the cells are capable of promptly disposing of the dye that might leak from the vessels. However, as to the origin and destiny of the cells which apparently differ from the epithelial cells of the stria vascularis, little was learned.

Another characteristic noted was that: when a preparation of the spiral ligament together with the stria vsacularis obtained from the animals that were injected only with the trypan blue solution was kept in formalin for a long time, the dye was unable to escape from the strial capillaries whilst dye within the small vessels of the spiral ligament was gradually lost. Thus, the blue network of the strial capillaries was embossed clearly (Fig. 7).

Other Parts of the Inner Ear. By removing the bony capsule of the inner ear, the remainder of the membranous labyrinth was exposed. No coloring was found in the membrane of the semicircular canals, though retention of the dye within vessels was observed.

Membranous tissue of the cochear aqueduct was also not stained, but along the wall of V. vestibularis and its tributaries near macula utriculi and macula sacculi, coloring was presented. Contents of the utricle and saccule, however, were not blue.

Preparations of the paraffin sections of the inner ear revealed that the dye could penetrate the spiral ganglion and the trunk of the acoustic nerve in the modiolus (Fig. 8). Flecks of blue staining were

Fig. 5.—Stained cells in the stria vascularis. No dye escape is observable from the capillary. X 100

Fig. 6.—Stained cells in the vicinity of the strial capillary. X 400

Fig. 7.—Strial capillary filled with trypan blue. The dye in the vessels of the spiral ligament was lost. X 100

USL, upper spiral ligament. LSL, lower spiral ligament.
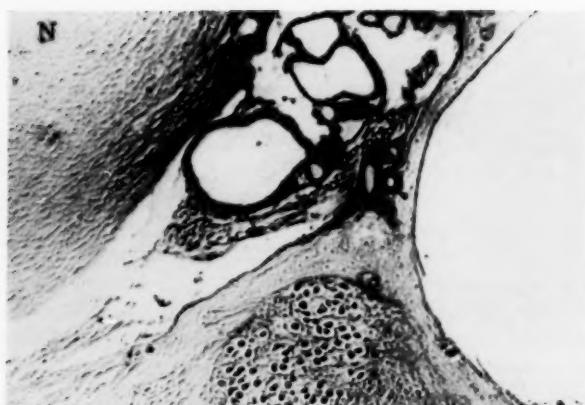
Fig. 8.—Penetration of trypan blue into the trunk of acoustic nerve.
N, N. cochleae in the modiolus.

observed within them. The outer part of the basilar membrane was
stained, but the organ of Corti was not. The walls of the "cavern-
ous" and "glomerulus" vessels, which Mygind called the vessels cours-
ing upwards with the nerve trunk in the modiolus and the tortuous
secondary coiled artery were darkly stained.

Brain. Cross sections of the brain showed deep blue coloring.
From the histological studies, it is confirmed that this was not due to
the dye that was contained within the brain vessels but to the staining
of the brain per se around the vessels. Permeation of the dye was
detectable throughout the brain, though trypan blue has been said
not to permeate the brain vessels except in certain areas. The type of
vessel that permitted dye penetration, however, was uncertain.

Kidney. The appearance and the cross sections of the kidney
showed blue coloring.

There were no remarkable changes in the glomerulus capillary.
In all cases, however, the epithelium lining Bowman's capsule was
colored blue, and particularly its nucleus was darkly stained. But
in cases of India ink injection, no dye was detectable out of the
glomerulus capillary. The capillary and other parts of the vessels
were full of India ink.

Fig. 9.—Dissected specimen of spiral ligament with stria vascularis. India ink injection. Figures correspond to those in description of comment. X 100

Dye penetration in the epithelial cells of tubules was occasionally observed in cases of trypan blue injection.

COMMENT

The distribution of small vessels is different in various organs. It may develop in a manner suitable for function of the organ. The vascular pattern in the spiral ligament of the cochlea is peculiar; roughly speaking, arterioles are found over the scala vestibuli, venules adjacent to the scala tympani. This must be taken into account in discussing the physiology of the cochlea.

According to Smith's observation,[2,3] the distribution of small vessels in the spiral ligament of the cochleae of the guinea pig, cat and the human is very similar. The small vessels in the spiral ligament together with the stria vascularis of the cochlea of the guinea pig are divided into five groups according to course and location (Fig. 9):

1. The vessels in the upper spiral ligament. These are the radiating arterioles over the scala vestibuli which derive from A. cochleae propria, and the capillaries which are branches from the arterioles.

2. The capillaries of the stria vascularis. These are true capillaries derived from arteriolar branches. The strial capillaries drain into the venules in the lower spiral ligament.

3. The vessels in the spiral prominence.

4. The venules in the lower spiral ligament.

5. The straight vessels in the thicker part of the spiral ligament. They course directly between arterioles in the upper spiral ligament and venules in the lower spiral ligament. They may be a kind of arteriovenous anastomosis.

The most serious objection to using dye in the experiment is that it is a foreign substance and toxic. However, the experimental procedure and criteria are not troublesome. Moreover, as trypan blue has been used in the experiments concerning the problem of labyrinthine fluids, it is not insignificant to observe the inner ear with the aid of dye injection from a viewpoint of capillary permeability.

Before discussing the results of the experiments, it is necessary to describe the architecture of the capillary wall.

The wall of the capillary is formed of a single layer of endothelial cells, intercelluar cement substance between them and basement membrane over the outer surface of the endothial tube. There is no difference in structures of endothelial cells of various tissues, so far as light-microscopical observation is concerned.

Electron-microscopical studies of the cerebral cortex and the hypothalamus of the rat have shown that the endothelium of the capillaries is a membranous structure about 1,500 Å thick with pores of several hundred angstrom in diameter. These transcapillary pores are tortuous in the cell and have openings towards both capillary surfaces (Fernández and Morán[1]). It is not elucidated, however, if the findings are applied for all of the endothelial cells.

The intercellular cement substance is supposed to be elaborated by the endothelial cell. It is chemically composed of chondroitin

sulfate which constitutes a mesh structure with pores 20 to 30 Å in diameter. Porous interstices vary with changes in the electrolytic balance of the medium. Moreover, blood protein is adsorbed on the internal surface of the capillary and serves to regulate the pore size of the cement filter. When calcium content or pH of the medium is decreased, the cement substance becomes unstable (Chambers and Zweifach[5]).

Basement membrane previously considered a homogenous layer has been demonstrated to be a fine fibrillar mesh buried in amorphous ground substance. The essential component of the basement membrane is hyaluronic acid which can be hydrolyzed and depolymerized by hyaluronidase. Therefore, the capillary wall becomes permeable to serum protein and colloidal dye.

The use of hyaluronidase, however, hardly produced extravasation of dye in the cochlea.

It has been known that an increase of capillary permeability occurs in the inflammatory process. Although it is still a matter of conjecture that histamine is the agent responsible for the phenomenon, histamine is considered to possess the .ability to increase capillary permeability. The action of ethyl alcohol and acetic acid on the capillary wall is quite different. Vonwiller[6] has shown that the mixed solution renders the capillary permeability abnormal, so that the ability of the blood-brain barrier to retain dye particles in the blood is lost.

This is explained from the characters of these agents. Ethyl alcohol may permit dye particles to penetrate the surface of the endothelium and the basement membrane. The injection of small quantities of acetic acid increases the acidity of the medium that in turn makes the capillary wall leaky. At any rate, with the aid of these agents, extravasation of the dye does occur whilst it hardly occurs without them.

The manifest coloring of the lower spiral ligament is due to the increased permeability of the venules that present adjacent to the scala tympani. Deep color at the part of attachment of the basilar membrane is partly due to the thickness of the spiral ligament.

Objection, however, may be raised to this interpretation of the phenomenon. It may not be extravascular leakage but absorption of dye particles into the venules from the perilymph to which dye

particles flow from the cerebrospinal fluid via the cochlear aqueduct
or directly from the small vessels other than venules in the cochlea.
Cerebrospinal fluid in the lateral ventricles and the cochlear aqueduct
was not colored blue. Pouring of dye into the scala tympani of the
basal turn did not take place through the opening of the cochlear
aqueduct.

Supposing that trypan blue intermingled rapidly with cerebro-
spinal fluid, the afflux of the fluid into the perilymphatic space
through the aqueduct takes a long time, as Arnvig,[7] Gisselson[8] and
Svane-Knudsen[9] have demonstrated.

The appearance of trypan blue in the scala tympani immediately
after the intracardial injection surely points to extravascular leakage
from the venules of the lower spi.al ligament.

Another route of dye leakage to the perilymph might be from
the small vessels proximal to the venules, but observations on the
radiating arterioles and capillaries which drain into the venules deny
this consideration.

The amount of the dye which leaked from the precapillary
bifurcation was very small. Furthermore, this is observed, though
to a lesser degree, without distinct change of color in the perilymph.

As constituents of the wall of the venules differ from those of
capillaries only in the muscle cells that are distributed sparsely outside
the endothelial tube, it is curious that leakage of trypan blue from
the strial capillaries hardly occurs.

Trypan blue has a comparatively small molecular weight
($C_{34}H_{24}N_6Na_4O_{14}S_4$, 960.83) but it has a tendency to form molec-
ular aggregates. Moreover, it is generally adsorbed in the plasma
protein in the blood stream. Therefore, trypan blue may be extraor-
dinarily large particles in the blood. The extravasation of India ink
from the venules has pointed to the conclusion that the vessels may
have pore membranes with large meshes.

Arnvig demonstrated the absorption of India ink that was in-
jected into the subarachnoidal space from the lower spiral ligament.
The present phenomenon is the reverse. Common is the demonstra-
tion of the perviousness of the venule wall to large particles of India
ink.

It is interesting to compare the staining of the cochlea with that of glomerulus in the same animal. Specimens from the animal injected with trypan blue solution show that the nucleus of Bowman's capsule was stained. This is surely suggestive of leakage of the dye from the glomerular capillary. On the other hand, in the case of India ink injection, no dye was detectable outside the wall of the glomerular capillaries, though it has not been decided that India ink never leaked from the glomerular capillary.

Electron-microscopical studies by Hall[10] have revealed that the wall of the glomerular capillary possesses layers of porous membrane, Lamina densa and lamina fenestrata with pore size of 50 to 150 Å and 1000 Å respectively. Pores of the venule wall of the lower spiral ligament are larger in diameter than those of glomerular capillary.

According to Starling's hypothesis,[11] the entrance and exit of materials through the wall of any small vessel are based on differences of hydrostatic pressure between both sides of the wall on one hand and of the colloid osmotic pressure on the other. This hypothesis was demonstrated by Landis[12] in the frog and Pappenheimer[13] in mammals. Water and water soluble materials are considered generally to be absorbed through the venule wall into the blood. The present experimental data seem to contradict the hypothesis.

Chambers and Zweifach were of the opinion that histamine produced arteriolar dilatation and increased the blood flow through the subordinate capillary bed. Using this concept, the mechanism of dye escape through the venule wall is explained by two changes as follows: the increased hydrostatic pressure of the circulating blood that is produced by histamine or ethyl alcohol-acetic acid solution and the increase in porosity, which is also brought about by the agents.

As the strial capillaries have higher hydrostatic pressure than the venules, dye escape may easily occur. Changes in the porous interstice of the strial capillaries or of the blood-stria barrier, however, may hardly become large enough to permit dye escape from them.

References to dye escape from the venules have been presented. Rous[14] and his associates have shown this escape in experiments on the sheet muscles of the guinea pig and the young rabbit. From experiments on the capillaries of the large omentum, Amano[15] has come to the conclusion that the outside migration of leucocytes occurs through the wall of venules, not through the capillary wall. Further-
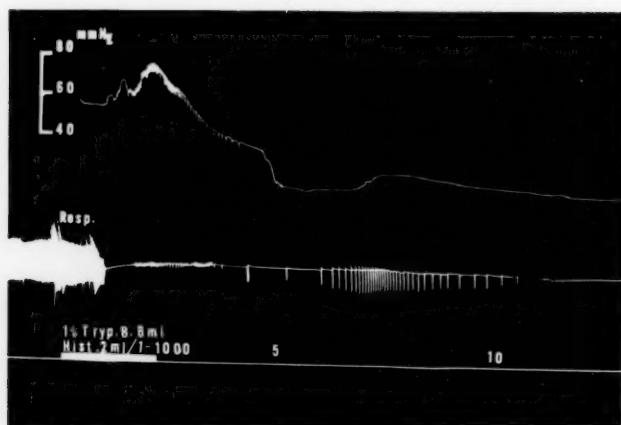
Fig. 10.—A change in the blood pressure and the breathing during the
vital staining.

more, he has shown extravascular leakage of India ink and trypan
blue through the wall of the venules under nearly physiological condi-
tions.

In the otological field, Kikuchi[16] has reported the perviousness
of the venules in the mucous membrane of the tympanic cavity to
India ink in the experimental otitis media induced by injection of
staphylococcus aureus or silver nitrate solution into the tympanic
cavity of the rabbit.

It was uncertain in the experiment of the inner ear if blood
corpuscles migrated outwards from the venules into the lumen. Dia-
pedesis may occur from the venules into the perilymphatic space of
the scala tympani.

The experiment showed increased perviousness of the venules
towards the basal coil. The suggestion is offered that permeability
dysfunction may be a causative factor of inner ear diseases in which
patients suffer frequently from hearing impairment with high tone
loss.

In contrast to the lower spiral ligament, coloring of the lateral
wall of the scala vestibuli is infrequently seen. The common concept

of the arteriole does not apply for the radiating arteriole over the scala vestibuli near the stria vascularis. Arteriole generally means a small supplying vessels with thick muscle layer of 20 to 50 μ in diameter. The radiating arteriole with the sparsely spread muscular cells is preferably called metarteriole or precapillary. Extravascular leakage of the dye from the vessels where precapillaries bifurcate may be due to mechanical factors, such as increased blood pressure or vortex formation in the blood stream. An example of change in blood pressure during the intra vital staining is shown in Figure 10.

In the stria vascularis, small amounts of trypan blue may pass through the capillary wall, though no dye was observed outside the capillary.

Experiments with fluorescein indicate that the dye is not impassable in the strial capillary as Gisselson has already demonstrated. The dissimilar results may be due to the difference in molecular weights and physicochemical properties of the dyes in the blood. Fluorescein has advantages for the experiment chiefly because of its low toxicity and of its relatively small molecular weight ($C_{20}H_{12}O_5$, 332.30), but permeation of fluorescein is so sensitive that its use to researchers for capillary permeability is not always suitable.

The pore system of the stria vascularis or of the blood-stria barrier barely permits trypan blue to escape. Leaked dye particles, however, may be rapidly disposed by phagocytes which were observed as stained cells in the vicinity of the strial capillaries. Usually, because of large amount of dye in the cell, details of the cellular elements were not observable.

Vital staining of the rats with trypan blue was performed by Spector.[17] He found blue stained histiocytes in the labyrinthine wall, basilar membrane, modiolus and within the tunnel of Corti.

Rüedi[18] inferred from the experiments with acoustic trauma that the stria vascularis possessed phagocytic processes.

The stria vascularis is endowed with the power of disposing of waste products. The work of the cells resembles the role of the astrocytes in the brain. Farquhar and Hartmann[19] have demonstrated by electron-microscopy that all the capillaries in the brain were surrounded tightly by the processes of the astrocytes, and that materials

when once passed through the capillary wall might spread along the processes of the astrocytes towards cell components.

Clemente and Holst[20] pursued in the monkey the relation of trypan blue penetration and the brain injuries produced by x-ray irradiation. They found that the extension of trypan blue penetration in the brain was the same as that of the destroyed astrocytes near the capillaries.

However, in the stria vascularis, the appearance of the cells is relatively small in numbers and dye escape does not occur without them. Consequently, their function is not to hinder dye escape but to dispose of the escaped dye.

From King's hypothesis,[21] the blood-brain barrier phenomenon is dependent upon the scarcity of connective tissues in the brain. In other organs injected dye penetrates into the connective tissues with or without penetration of the parenchyma. Edström[22] elucidated the barrier phenomenon from the effect of cell membrane that was closely adjacent to the wall of the brain capillary.

The pavement of marginal cells closely contacted with the strial capillaries may indicate the scanty ground substance in the stria vascularis. One must, however, be careful in deciding the site of blood-stria barrier.

Many investigators have long since discussed the source or origin of the peri- and the endolymph.

Perilymph communicates with the subarachnoid space via the cochlear aqueduct, though a few investigators have claimed other communications. By tracing iron salts injected in the cerebrospinal fluid of the cisterna magna, the circulation of the cerebrospinal fluid and the perilymph was studied in the guinea pig, the rabbit, the cat and the monkey.[23] They reported that a part of the salts entered into the perilymphatic space via the cochlear aqueduct, then they went laterally into the lower spiral ligament and were resorbed into the blood vessels.

Svane-Knudsen has come to conclusion that resorption of the cerebrospinal fluid takes place from the vas scala angularis.

However, Gisselson has demonstrated in the cat that fluorescein injected intravenously does not enter the perilymphatic space for

hours if the inner ear is kept intact, notwithstanding the fact that it penetrated the blood-cerebrospinal fluid barrier and intermingled with fluid.

Altmann and Arnvig have expressed the opinion that open communication existed between both spaces but fluid displacement hardly occurred. Kley[24] observed filling of the fluid in the perilymphatic space of the guinea pig in spite of the complete obstruction of the cochlear aqueduct.

It is impossible to view the cerebrospinal fluid as the sole source or origin of the perilymph in certain animals and in man where communication through the cochlear aqueduct is doubtful.

Recently, the theory of double sources has prevailed, viz., the fluid comes partly from the cerebrospinal fluid and partly from the wall of the perilymphatic space.

Mygind[26] considered that the perilymph was produced by filtration from the capillary network of the upper spiral ligament and resorbed from the spiral ligament closely under the basilar membrane. Rüedi supported the theory of double sources from his experiments using radio-isotopes in the guinea pig. Miyake[26] demonstrated that p^{32} labelled phophate injected intracardially appeared in the perilymph after a short period of time in spite of the obstruction of the cochlear aqueduct. Furthermore, from the quantitative analysis of Na and K, and the observation of the crystal patterns, he asserted, also, the theory of double sources.

There are no glandular cells in the wall of the perilymphatic space. Therefore, if the perilymph is given off by secretion, it involves the active transport of materials by mesothelial cells with energy consumption. On the other hand, if the formation is due to ultrafiltration, the present data are indicative of its sites.

Materials of small molecules and occasionally large molecules are expected to be filtered through the vessels where precapillary vessels ramify.

The chemical composition of the perilymph is similar to that of the cerebrospinal fluid, but not identical. The difference of protein contents of the two fluids is remarkable. It is greater in the perilymph than that in the cerebrospinal fluid.[27-29] Protein in the perilymph, from the viewpoint of ultrafiltration, probably comes from the blood

through the just mentioned vessels in the upper spiral ligament and venules in the lower spiral ligament, as these vessels are proven to possess walls pervious to large molecules.

Another probability is that the perilymph is derived from the endolymph through the wall of the membranous labyrinth. According to Max Meyer's observation,[30] the wall of the membranous labyrinth is pervious to small molecular substances in both directions. Kley, also, has maintained that there is a source of the fluid from the endolymphatic system besides the partial formation from the capillary in the wall of the perilymphatic space. Altmann and Waltner[23] indicated perviousness of the basilar membrane to trypan blue. But in the present experiment, dye was not detectable in the membranous labyrinth and within the ductus cochlearis, except the outer part of the basilar membrane.

Regarding the absorption of the perilymph, the data present suggestion. The findings observed in the lower spiral ligament of the basal coil indicate the existence of a specific perivascular space around the venules, though it is not confirmed that the space exists in other coils. Normally, tissue fluid probably flows from the space into the modiolus. Absorption of the fluid in the cochlea may take place partly in the space in the lower spiral ligament of the basal coil.

The source or origin of the endolymph, too, has been a controversial matter. From histological grounds, A. Saxen and v. Fieandt[31] surmised the stria vascularis and the external spiral sulcus as the site of secretion and resorption of the endolymph. Experiments with p^{32} carried by Rüedi led to the same results. Another theory of the endolymph formation in the cochlea is that the fluid is derived from the perilymph through Reissner's membrane.[32]

The present data are not useful to conjecture the source or origin of the endolymph in the cochlea.

It is known that the blood vessels are pervious to the dye in certain regions of the brain, such as the pineal body, area postrema, tuber cinereum, posterior lobe of the hypophysis, paraphysis, wall of the optic recess and eminentia saccularis of the hypophyseal stem (Davson). These special areas of the brain are considered to be relevant to secretory functions or located contiguous to the region that produces the secretion. Absent or reduced blood brain barrier is favorable for the secretory cells to catch rapidly the changes in the chemical compositions of the blood.

The findings of the stria vascularis are, however, not incompatible with the secretory activity of the stria vascularis. The strial capillaries are closely surrounded by epithelium in which the constituent cells may absorb selectively materials from the blood into the cytoplasm and expel them to the endolymph. Differing from the regions of the brain, the secretory cells of the stria vascularis may not necessarily be influenced by changes in chemical compositions of the circulating blood. To maintain the components of the endolymph constant, the existence of a strong barrier must be convenient for the secretion of the fluid.

It is dangerous to decide the physiology of the labyrinthine fluids from the experiment. However, another interesting problem is offered: What kind of factors are necessary to permit passage of materials freely from the blood to the endolymph?

SUMMARY

Permeability of the cochlear vessels is studied with the aid of vital staining of the guinea pig.

1. In the stria vascularis, a high potential-barrier exists between the blood and the tissue. The restriction of the escape of dye from the blood in the stria vascularis is more prominent than that in the brain. This is probably favorable to maintaining the components of the endolymph constant.

2. The stria vascularis possesses the function of disposing of foreign substances and probably of waste products. Phagocytes probably settle in the stria vascularis and play a role in the process.

3. Dye escape hardly occurs in the endolymphatic system whilst it easily occurs in the perilymphatic space especially through the venules in the lower spinal ligament.

4. The sources or origins of the labyrinthine fluids are discussed from the viewpoint of the permeability of the vessels.

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THE ROLE OF NUTRITION IN ORAL LEUKOPLAKIA

INCLUDING A THERAPEUTIC TRIAL OF TOPICAL VITAMIN A

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Leukoplakia of the oral cavity is a condition of particular significance because of the frequency with which malignant change occurs in the abnormal tissue. Weisberger,[1] for example, records a series of 275 patients with oral carcinoma, of whom 60 per cent developed the malignancy at the site of leukoplakia. Wynder and Bross[2] reported leukoplakia present in 45 per cent of 52 patients with cancer of the buccal mucosa. The observation of this progression from a benign to a malignant lesion is sufficiently common as to be an undoubted part of the natural history of the disease.

The cause of the oral leukoplakia however remains obscure. Epidemiologic studies[1,2] show a rather constant association of the condition with heavy smoking, alcoholism and syphilis and other environmental factors have been suspected, such as various dental conditions leading to local trauma. However, no basic mechanism leading to the development of leukoplakia has been found. For reasons which will be discussed, nutritional deficiency has been a popular suspect for a long time and the standard clinical approach to leukoplakia is to ensure that no frank malignant lesion exists which might require surgical removal and then to advise a reduction in smoking and the taking of some form of vitamin therapy. In particular, vitamin A or the B vitamins are commonly used. However, few clinicians can be satisfied with these methods since cures are rather uncommon and the development of malignant change often continues inexorably in spite of all conservative treatment.

Mulay and Urbach[3] reported in 1958 that they had considerable success in treating oral leukoplakia with a troche containing 150,000 units of vitamin A, seven of ten patients in their group showing "very

marked improvement." Because of the lingering doubt about the role of nutritional deficiency in causing leukoplakia, it was decided to re-examine the concept in a group of patients who were not overt alcoholics and to use the same group, after adequate work-up, to carry out a double-blind study of the same vitamin A containing troches reported beneficial by Mulay and Urbach (loc cit).

<div align="center">PROCEDURE</div>

1) *Patients*. A total of 34 patients with filed diagnoses of "leukoplakia" in the records of Memorial Center were asked to co-operate in the study. Eight of these were judged to be unsuitable for the therapeutic trial after examination, leaving 26, half of each sex. Table I provides a description of this experimental group and the site and extent of their lesions and pathological reports if a biopsy had been carried out. It should be pointed out that although 13 (50%) of the patients did not have biopsy confirmation of leukoplakia, all had been independently diagnosed as such before admission to the study.

2) *Nature of Investigations*. Patients identified in the above way were seen at a special study clinic. At the first appointment a detailed history of the oral condition was taken, followed by a general medical history and a physical examination including evaluation of nutritional status from a clinical standpoint, general routine examination of systems and a specific examination of the oral cavity. Oral lesions were photographed in color at the first visit and at selected times during the follow-up period. In addition, at the first visit, an experienced interviewer obtained information on selected environmental factors, notably smoking habits, alcohol intake, oral hygiene, medications and x-ray exposure. Ten patients had blood drawn for the determination of plasma, vitamin A and carotene levels. Finally, 19 patients kept a detailed record of all food eaten during seven consecutive days, quantities being estimated in domestic units as accurately as possible. This record was then used as a basis for an interview during which an experienced nutritionist sought to cross-check the food intake both qualitatively and quantitatively. Food models were used to help in this process. The opportunity was also taken to try to define any ways in which long-term dietary intake might differ from that recorded and also to be certain that the presence of an oral condition was not conditioning the diet currently eaten. A dietary pattern was thus established which it was felt represented, as accurately as possible, the long-term intake of the subject and this was transposed into specific nutrients for comparison with

TABLE 1

DESCRIPTION OF PATIENT SAMPLE BY SEX, AGE AND LESION

SEX	NO. OF PTS.	AGE RANGE AND MEAN	SITE OF LEUKOPLAKIA*			EXTENT OF LEUKOPLAKIA			BIOPSY REPORT:			
			Buccal Mucosa	Tongue	Palate	Very Local	Moderate	Diffuse	Hyper-plasia	Leuko-plakia	Leuko-plakia and Ca.	None
FEMALE	13	39-78 57	8	6	0	4	8	1	1	2	2	8
MALE	13	41-70 55	8	5	2	4	7	2	1	5	4	3
TOTAL	26	39-78 56	16	11	2	8	15	3	2	7	6	11

* N.B. Three patients had lesions at two sites simultaneously.

a standard provided by the Recommended Dietary Allowances (R.D.A.).[4]

Following the above initial work-up, patients were given supplies of troches with instructions to dissolve one in the mouth three times a day after meals. These were distributed alternately by sexes so that half of each group received a troche containing 150,000 units of synthetic vitamin A and the other half an identical troche without vitamin A. The double-blind principle was used. Patients were subsequently seen at intervals of about two months to assess progress and re-photograph lesions as necessary.

<div align="center">RESULTS</div>

1) *Clinical Evaluation.* General physical examination of the study group provided no suspicion of clinical conditions which might be related to leukoplakia. Family histories were negative except for one instance of a sister reported to have leukoplakia. An attempt to see this relative was not successful. Three patients gave histories of syphilis which may well have been significant in the etiology of their leukoplakia.

The striking thing about the oral lesions was the greatly variegated naked-eye appearance that "leukoplakia" presented. At least three basic types can be classified:

   a) So-called "filmy" leukoplakia which is always in the lateral buccal cavity and presents as a semi-opaque white sheet, with a loss of the natural sheen. The affected area is always normal to palpation.

   b) A more demarcated, elevated and palpable white plaque-like lesion presumably true "leukoplakia."

   c) A granular, rather reddish lesion which is indurated but not elevated to palpation. This appearance seemed to be associated with a likelihood of current or subsequent malignant change.

Two patients had coexistent lesions of the filmy and plaque-like types and two more had coexistent plaque-like and granular types, suggesting the possibility of a common etiology. However, in 22 of the patients (85%) only a single type of lesion was seen. Because of the relatively small sub-groups involved, analysis of the data on types of lesion in relation to interacting factors is difficult to interpret with certainty. Table II presents some figures on sex, site, pathology

TABLE II

TYPE OF LESION IN RELATION TO SEX, SITE, PATHOLOGY AND RESPONSE TO THERAPY

TYPE	NO. OF PTS.	SEX		SITE[1]			POSITIVE BIOPSY REPORT		THERAPEUTIC[2] GROUP		RESPONSE TO THERAPY	
		Male	Female	Buccal	Tongue	Palate	L/P only	L/P & Ca.	Vit. A	Placebo	Obj. Imp.	No. Imp.
Filmy	8	2	6	8	0	0	3	0	7	4	1	7
Plaque-like	15	9	6	6	10	2	4	4	7	9	4	11
Granular	3	2	1	2	1	0	0	2	2	2	0	3
TOTAL	26	13	13	16	11	2	7	6	16	15	5	21

[1] Three patients had lesions at two sites.

[2] Thirty-one treatments to 26 patients.

TABLE III

TOBACCO AND ALCOHOL CONSUMPTION OF LEUKOPLAKIA PATIENTS

SEX	NO. OF PTS.	TOBACCO CONSUMPTION: LONG-TERM				AFTER ONSET OF LEUKOPLAKIA				LONG TERM INTAKE OF ALCOHOL:			
		None	Low	Mod.	High	None	Low	Mod.	High	None	Low	Mod.	High
FEMALE	13	4	0	8	1	6	2	5	0	6	5	2	0
MALE	13	1	0	5	7	3	3	7	0	2	3	6	2
TOTAL	26	5	0	13	8	9	5	12	0	8	8	8	2

and response to therapy of the three types. Filmy leukoplakia was relatively more common in the women, occurred entirely in the buccal cavity and was never associated with malignant change. Biopsy was carried out in only three of the eight patients because of the recognized benignity of this type of lesion. Plaque-like lesions occurred more frequently in the men and were somewhat more frequent on the tongue than the buccal mucosa. Eight of fifteen cases were biopsied, four being reported as leukoplakia alone and four leukoplakia with epidermoid carcinoma. Two of the three patients with granular lesions had malignant change. There was no clear-cut relationship of type of lesion with tobacco or alcohol consumption.

2) *Environmental Factors.* Table III summarizes the tobacco consumption of the group by sexes. Tobacco consumption is defined at four levels and over two phases, long-term consumption prior to the onset of leukoplakia and consumption after diagnosis, when habits are frequently modified. Low consumption is considered equivalent to smoking 10 cigarettes a day or less, moderate consumption 10 to 40 cigarettes a day and high consumption 40 or more cigarettes a day. Among the 12 men who were classified as having moderate or high tobacco consumption, only three were pure cigarette smokers, two smoked cigars only and the other seven smoked various combinations of cigarettes, cigars and a pipe. Fewer women had a high consumption of tobacco by our classification, but eight of the thirteen smoked 10 to 40 cigarettes a day. Four women and one man had never smoked. Tobacco consumption tends to be reduced after the diagnosis of leukoplakia, presumably because of the advice given by physicians, but almost half of the total group remained "moderate" smokers.

Alcohol consumption in the study group is also presented in Table III and is defined at four levels. Low consumption means the taking of alcohol only occasionally, generally for social purposes. Moderate consumption means the regular daily consumption of alcohol but in purportedly modest quantities equivalent to a maximum of perhaps two "shots" of liquor before dinner. Anything in excess of this arbitrary daily level is considered high consumption. Six men and two women are thus classified as moderate drinkers and two men as heavy drinkers. In contrast to tobacco, there was no evidence that alcohol consumption was reduced after the diagnosis of leukoplakia. This may represent differences in true "addiction" to the habit or differences in the degree of emphasis placed upon tobacco and alcohol as etiologic agents by the physician.

3) *The Evaluation of Nutritional Status.* Of the 26 patients seen in this study, only two presented clinical findings suggesting the possibility of malnutrition. Both were postmenopausal women with the edentulous state, drooping mouth, angular stomatitis, pallor and anemia which are often associated with iron-deficiency. However, neither had dysphagia, koilonchia or smooth tongue. The diet of one was evaluated as below 80 per cent of R.D.A. in calcium, iron, vitamin A and thiamine. The ascorbic acid intake appeared to be very low. The other patient had a satisfactory diet in all nutrients except vitamin A. Both, however, had taken multi-vitamin supplements over long periods of time without any change in their general condition or their leukoplakia. It seems likely that their condition was that described by Pollack[11] as pseudoariboflavinosis, in which the lack of dentures is held to cause a narrowing of the intra-maxillary space with subsequent mechanical drooping of the mouth and stomatitis. Both were probably mildly iron-deficient but leukoplakia has not been reported as associated with that condition although atrophic changes in mucous membrane and subsequent malignant change may be.

Except for the two patients discussed above, the remainder of the study group appeared to be well-nourished and 17 (or 65 per cent) were obese. Additional data on the estimated intake of specific nutrients are presented in Table IV. This shows an analysis of the intakes of certain specific nutrients in relation to the Recommended Dietary Allowances (R.D.A.)[4] for the 19 individuals concerned. Three levels of intake are indicated, namely 50% or less of R.D.A., 50% to 80% of R.D.A., and 80% or more of R.D.A. These permit different degrees of confidence in the interpretation of results. Few authorities would suspect a significant deficiency of a nutrient above

TABLE IV

RELATION OF INTAKE OF SPECIFIC NUTRIENTS TO RECOMMENDED
DIETARY ALLOWANCES (R.D.A.)
(in 19 of 26 patients)

NUTRIENT	Protein	Calcium	Iron	Vit.A	Thiamine	Ribo-flavin	Niacin	Ascorbic Acid
Number of subjects with intake:								
More than 80% of R.D.A.	19	13	14	12	11	18	19	11
50 to 80% of R.D.A.	0	5	5	7	7	1	0	5
Less than 50% of R.D.A.	0	1	0	0	1	0	0	3

80% of the R.D.A. and in the 50% to 80% range the significance would be in doubt, having regard to the margin of safety incorporated in the allowances. However, between five and seven individuals in the study apparently had intakes in the 50% to 80% range for the individual nutrients calcium, iron, vitamin A, thiamine, and ascorbic acid. Below 50% of R.D.A. a deficiency is much more likely to be of significance. In this range we find only one instance of low calcium and three of low ascorbic acid intake. In terms of the nineteen subjects on whom dietary intake data were obtained, only four met the R.D.A. in all nutrients, six having intakes lower than 80% of R.D.A. of a single nutrient, four of two nutrients and the remaining five of three or more nutrients. It should be noted that nine of the 19 patients studied in this way took, or had taken, vitamin supplements for significant periods of time after the diagnosis of leukoplakia and the intakes calculated and reported in Table IV do not include such sources.

The only biochemical test applied to the group was the determination of vitamin A and carotene levels in plasma from ten subjects and these were, in all cases, either high normal or above normal. The latter state presumably reflected concurrent vitamin supplementation.

The final interpretation of these dietary data is difficult since no control group is available for comparison. However, it was the

strong impression of the nutritionists who carried out the dietary evaluation that the intakes of the group as a whole were very similar to those they encountered regularly in hundreds of subjects without leukoplakia who were seen in connection with the regular work of the Health Center. The uninitiated must certainly be warned that failure to meet the R.D.A. in one or more nutrients is very common and that even the intake of less than 50 per cent of the R.D.A. of any nutrient may not be associated with demonstrable ill-effects.

4) *Therapeutic Trial of Vitamin A Troches.* For the purposes of the therapeutic trial patients were divided by sexes, each group receiving troches on the double-blind principle, the placebo and vitamin A-containing preparations being given alternately under a code unknown to the patient or investigator. An analysis of the resulting "vitamin A" and "placebo" groups shows no significant difference in mean age, duration and site of lesions, smoking or alcohol intake. Table II shows a preponderance of plaque-like lesions in the placebo group as opposed to the vitamin A group where filmy and plaque-like types were of equal incidence. Table V shows that the duration of therapy varied from seven to 52 weeks in the patients of both groups, with a mean of about 20 weeks in each case. Experience with the two groups was very similar in all respects except one. In both groups about 60 per cent of the patients got neither worse or better, subjectively or objectively, while under treatment. Another 12 to 20 per cent showed deterioration. Three patients in the placebo group showed some improvement but this was objective in only one. In the vitamin A group, however, four patients showed objective improvement and this was of significant degree in three, one of whom demonstrated the only "cure" in the study. However, all three patients in question had made a significant reduction in their use of tobacco immediately prior to entry into the study or during its course and the cure occurred in a man who stopped smoking completely, after 20 years of smoking 30 cigarettes a day. This change of habit occurred just before his admission to the study, upon the advice of his physician because of a recent coronary occlusion. Under such circumstances, of course, it was not felt that smoking habits could be controlled for the sake of the study. Nor could other subjects be discouraged from reducing their use of tobacco, if they had been so advised, especially when a potentially pre-malignant condition existed.

Objective improvement following therapy occurred more frequently with the plaque-like lesions than the other two types (Table II) but with the small numbers involved, and other factors such as

TABLE V

RESULTS OF THERAPEUTIC TRIAL

(31 Treatments to 26 Patients)

THERAPY GROUP	SEX	NO. OF PTS.	MEAN PERIOD OF THERAPY (weeks)	PROGRESS DURING PERIOD OF THERAPY:							
				IMPROVEMENT					NO CHANGE	DETERI- ORATION	POSSIBLE SIDE EFFECTS
				Subjec- tive only	Slight	OBJECTIVE		Total			
						Moderate	Cure				
PLACEBO	F	8	20 (8-39)	0	1	0	0	1	5	2	2
	M	7	23 (9-52)	2	0	0	0	0	4	1	0
	Both	15	22 (8-52)	2	1	0	0	1	9	3	2
VIT. A	F	8	15 (8-24)	0	0	0	0	0	7	1	4
	M	8	24 (7-45)	1	1	2*	1**	4	2	1	1
	Both	16	19 (7-45)	1	1	2*	1**	4	9	2	5

N.B. 5 pts. observed for adequate periods of both placebo and vit. A troches.
  * Significantly reduced smoking during Vit. A therapy.
 ** Completely stopped smoking prior to Vit. A therapy.

smoking habits apparently playing an important part, this may be
of no significance. On the whole the results of the therapeutic trial
are felt to be entirely negative in view of the fact that almost 80 per
cent of those using the vitamin A containing troche were either unim-
proved or got worse. If filmy and granular types are excluded there
is a possibility that the vitamin A troches were beneficial, however
the complication of change in smoking habits again arises. Any
change noted in the patients of both groups is felt to be largely due
to the apparently random fluctuation of leukoplakia under many un-
known influences, the one consistently beneficial factor being a reduc-
tion in smoking. Where deterioration was noted, either objectively
or subjectively, side effects due to the troches may have been respon-
sible in some measure, although this cannot be inferred with any
certainty. Four episodes in three patients suggested an allergic reac-
tion with swelling of the lower lip or the peri-orbital region and two
such cases were actually observed. A further four patients developed
soreness of the mouth or throat. In four cases these symptoms
eventually necessitated withdrawal from the study. The other four
patients subsequently tolerated the treatment and remained actively
involved. These episodes occurred about equally on the vitamin and
the placebo troches.

COMMENT

The first observation which has been made is that leukoplakia
is commonly a very ill-defined entity, both in gross and microscopic
appearance. The clinician tends to label all hyperkeratotic white
patches in the mouth by this name and thereafter is forced to consider
all such lesions as potentially pre-malignant. One suspects further-
more that the submission of biopsy material with the clinical diagnosis
of leukoplakia will often evoke a confirmatory pathological diagnosis
if hyperkeratosis is seen by the pathologist. However, Bernier[5] and
Shira[6] have stressed the need for discrimination between hyperkera-
tosis and dyskeratosis, the latter implying a disorder of maturation of
the epithelium identified by changes in the morphology and staining
characteristics of cells of the basal and prickle-cell layers. When
these changes are seen a pre-malignant lesion, true leukoplakia, is
said to be present. Hyperkeratosis, or the excessive presence of
keratin, is not alone considered enough evidence to justify the diagnosis
of "leukoplakia" and the term "pachyderma oralis" has been coined
to describe the simple hyperkeratotic and basically benign lesions
said to result from chronic irritation.

The final validation of these hypotheses can only come from a
detailed, prospective study of the natural history of an adequate num-

ber of patients with leukoplakia-like lesions in their mouths, and no such project has apparently ever been carried out. The present study can only confirm that lesions labelled as leukoplakia by clinicians, and often confirmed as such by pathologists, can have a wide variety of naked-eye appearances and very different paths of natural development, at least as judged by the rate of progression or nonprogression to malignancy. It is reasonable to suppose that the different lesions, if they exist, will also have different etiologies and different responses to various therapeutic approaches, a fact which must confuse all studies without rigid diagnostic criteria.

The factors most popularly considered to bear some etiologic relationship to oral leukoplakia are chronic irritation, e.g., from a badly fitting dental plate or a jagged tooth, syphilis, alcoholism, tobacco and specific or non-specific malnutrition. It is worthwhile to see in what ways the observations made in the present study bear upon these possibilities. Chronic irritation of a mechanical nature was not apparent in any case seen, although well-defined cases of hyperkeratosis adjacent to a sharp or jagged surface apparently occur. Bernier (loc cit) would classify these as pachyderma oralis and not leukoplakia. Eighteen of the patients in our series (or 69 per cent of the group) had diffuse lesions in which local trauma could not be an operative factor. Chemical irritation and poor oral hygiene have also been considered as causative circumstances, but it is difficult to see how these could be assessed. Three patients seen in the study gave a past history of syphilis and in all cases this was of long duration, requiring recurrent treatment. Presumably this was of etiologic significance, although only one of the three had the leukoplakia on the tongue, which is the characteristic site.

The relationship of alcoholism to oral leukoplakia has been documented in several reports such as those of Wynder and Bross[2] and Trieger and co-workers.[7] The series used in the present study cannot be considered random since overt alcoholism was considered a disqualifying factor. Despite this, however, the data in Table III show that ten patients out of twenty-six (39%) were steady drinkers of alcohol although often in apparently moderate amounts. None would have attracted attention as being alcoholic by their general appearance. In alcoholics it is possible that nutritional factors could be operative, although with one exception, those patients with a steady intake of alcohol in the present study appeared to have dietary intakes similar to the others. Neither did their lesions improve with vitamin therapy systemically or topically. The presence of substantial numbers of alcoholics in any hospital population of patients with

leukoplakia is certain to provide a number who look malnourished. It is only clear that many otherwise similar patients do not look that way or present any other evidence of malnutrition. The problem in this regard, as in others, is the lack of any acceptable control group.

The relationship of smoking to leukoplakia is more certain in the writer's opinion, although the presence of five non-smokers in our 26 cases shows that similar lesions can occur without this environmental factor. Four of these five were women whose leukoplakia developed after the menopause and the fifth was a man with a tongue lesion, repeatedly reported as leukoplakia on biopsy and with the eventual development of malignant change. This patient had not had syphilis. The other 21 patients were all originally moderate to heavy smokers. The majority of these claimed to have reduced their use of tobacco after the diagnosis of leukoplakia was made and many recognized co-incident improvement in their lesions. Three patients were seen to improve while being followed on the therapeutic trial and during periods of substantial reduction in tobacco usage. However, three other patients stopped smoking many years before the start of the study without subsequent improvement and two of these patients later developed malignant lesions in the affected areas. It is apparent therefore that smoking is not an essential factor in the development or the maintenance of leukoplakia and, having regard to the relative infrequency of leukoplakia when compared to the number of heavy smokers in the population, it may be a co-factor requiring some other specific condition to be active. Mellors[8] has demonstrated differences between the mucous membrane from patients with leukoplakia and that of normal subjects in the development of intracellular fluorescent bodies when exposed to cigarette smoke. The significance of this observation is uncertain, but it does indicate that the existence of leukoplakia may modify the effects of smoking. Goldhaber[9] has also shown by a fluorescent technique that there is essentially no penetration of normal mucous membrane by a carcinogen, methylcholanthrene, but that absorption occurs where there is hyperkeratinization.

Particular attention was given to the nutritional status of the patients in the present study because of the frequently expressed opinion that leukoplakia can be due to malnutrition. Such an association seems plausible when one considers 1) that certain deficiency states, e.g. of B-group vitamins and iron[10] cause changes in oral mucous membranes; 2) that leukoplakia appears to be more common in chronic alcoholics, whose nutritional status is always suspect, and 3) that leukoplakic lesions sometimes appear to improve on vitamin therapy. The findings of this study, however, fail to support the

hypothesis that nutritional factors, at least of a conventional nature, are of primary importance in the etiology of this condition. Neither clinical examination nor a careful evaluation of nutrient intake suggested any consistent pattern of deficiency. The majority of the patients seen had taken vitamin supplements, often in large dosage and for long periods, but only one claimed sustained benefit from such therapy. It seems likely that when a leukoplakic lesion shows improvement with vitamin therapy this is either a part of the spontaneous regression and remission which may occur or, more frequently, results from a coincident reduction in tobacco usage. Mulay and Urback (loc cit), who reported beneficial effects with vitamin A troches, do not mention this possibility and their study unfortunately had no control group or the safeguards of the double-blind principle.

Finally one may add some more indirect evidence against the hypothesis that vitamin deficiency is a primary factor in the causation of leukoplakia. On theoretical grounds alone the failure to respond to vitamin therapy is suggestive, but the possibility of an irreversible change in the tissues following a period of deficiency exists. On the other hand no deficiency state known to the author produces hypertrophy in the human mucous membrane in contrast to atrophy, which is the common response. In such countries as Mexico, where diets are often low in protein and in many of the vitamins, including A and the B group, oral cancer is said to be common but rarely secondary to leukoplakia.[12] Recent nutrition surveys in Ecuador and Vietnam showed that local diets were frequently deficient in vitamin A, among other nutrients, but dental surgeons reported only two cases of leukoplakia in over 6,000 examinees.[13] Leukoplakia and primary malnutrition per se do not appear to be coincident in population groups.

The experience afforded by the reported study has convinced the writer that future work on this problem must proceed unhindered by many of the currently held, but poorly substantiated, views on etiology. If a nutritional deficiency is involved it must be of an obscure nature, i.e., involving a nutrient other than those commonly considered essential or, perhaps, some curious aberrant metabolic processes or uncommon tissue requirement. The commonly held role of a conventional vitamin-deficiency seems fallacious. The effect of hormonal mechanisms is unknown, although leukoplakia apparently occurs not infrequently in women before the menopause, if they are smokers. Quite clearly, future studies must be based on strict diagnostic criteria and an attempt should be made to learn the natural

116   JEFFREY H. FRYER

histories of true leukoplakia and the various leukoplakia-like syn-
dromes.

SUMMARY AND CONCLUSIONS

A study is reported in which 26 patients with a clinical diagnosis
of oral leukoplakia were evaluated for the possible significance of
nutritional factors in the etiology of their condition by means of a
clinical examination, a detailed dietary history (19 patients) and
the measurement of blood carotene and vitamin A (10 patients).
Additional observations on the use of alcohol and tobacco were also
made. Finally the patients were placed on a double-blind therapeutic
trial of a vitamin A containing troche previously reported effective.

The patient sample is described by age, sex, site and extent of
lesion and biopsy reports where available. The naked-eye appearance
of the lesions varied greatly and support is expressed for the view of
other writers that all hyperkeratotic lesions are not true leukoplakia.
Varying types of similar lesions may have different etiologies and
different natural histories with especial reference to malignant change.
There is urgent need for a prospective study in this area.

This study supported the common association of leukoplakia
with smoking and the observation that a reduction in tobacco con-
sumption is often, but not always, helpful to the patient. Overt
alcoholics were excluded from the study but several took alcohol
regularly in moderate amounts. The significance of alcohol intake
in this condition remains unknown.

No evidence was found to support the idea that conventional
nutritional deficiencies were of etiologic significance in this particular
group of patients. Reasons are suggested why vitamin deficiency
has been suspected as a cause of leukoplakia but these may be falla-
cious. Specific nutritional therapy appears to be ineffective and a
therapeutic trial of vitamin A troches reported by others to be help-
ful, failed to demonstrate any significant positive results.

21 DEVONSHIRE PLACE, W 1

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VIII

THE EFFECT OF RADIATION ON THE LARYNX
WITH PICTURES OF THESE EFFECTS

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AND

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Cleveland, O.

The purpose of this paper is to illustrate pictorially the effects that are visible in the larynx when it is irradiated for carcinoma. A thousand words cannot take the place of one picture.

In this paper we are concerned with the effect of radiation, not on the skin, but on the larynx and laryngeal structures. The ionizing effect of radiation is the same regardless of whether it is teleradium, x-ray, neutron bombardment, emanations from cobalt, or other source.[1] It has been found through experience over the years that 6000 to 8000 roentgen units, delivered to a laryngeal tumor, will effect the growth rate of that tumor.[2-4] This amount of irradiation, has an effect on the normal structures of the larynx, as well as on the tumor itself. A cancer killing dose of radiation, from whatever source, invariably leaves a residual effect in the larynx.

Of the cases to be presented, three were obtained from autopsy and two from laryngectomy, following what have been considered to be cancer killing doses of radiation to the larynx.

REPORT OF CASES

Case 1. K.L., a 55 year old white male, had dysphagia and hoarseness for four months. A lesion, which proved to be squamous cell carcinoma on biopsy, involved the right arytenoid and aryepiglottic fold. The patient refused surgery and radiation was initiated; approximately 7500 roentgen units (r) were delivered to the tumor through two portals measuring 6 by 5 cm from a 200 KV radiation unit at 18 milliamps, screened with 0.5 mm of copper plus 1 mm of aluminum, at a 50 cm distance. Eleven months later, due to increasing dysphagia and radiation reaction, the patient became dyspneic and

emergency tracheotomy was performed to provide an airway. A repeat biopsy was obtained showing recurrence of squamous cell carcinoma. Following the tracheotomy, the patient developed a large laryngo-tracheal fistula with multiple metastases to the cervical nodes, chest, right iliac crest, ribs, diaphragm, axillary nodes, and extension locally from the original lesion into the neck and pharynx. The patient expired 19 months following his radiotherapy. An autopsy was performed.

The specimen opened from behind is shown in Figure 1. There is present a marked deformity of the larynx with edema and swelling of the epiglottis and entire laryngeal area. The deformity and edema account for the difficulty in respiration which made the tracheotomy necessary.

Figure 1 also shows a section through the right side of the thyroid cartilage and illustrates radionecrosis of the thyroid cartilage, scarring, ulceration and debris, with recurrence of the tumor and generalized necrosis of the laryngeal surface. The tumor had not been eradicated by the radiation treatment.

CASE 2. J.O., a 66 year old white male, presented with a history of hoarseness and sore throat for two months. Laryngoscopy revealed a lesion involving the tip of the left arytenoid, the left side of the aryepiglottic fold and the lateral wall of the hypopharynx. Biopsy showed a poorly differentiated squamous cell carcinoma. Surgery was refused and radiation with the same factors as in Case 1 was given in 40 doses through a single 6 by 5 cm field over the left hypopharyngeal area covering approximately 50 days. The patient was admitted four months later with marked dyspnea. A tracheotomy was performed and a feeding tube inserted because of difficulty in swallowing. Seven months from the time of the start of irradiation, the patient developed a massive hemorrhage from the tracheotomy tube and mouth, due to rupture of the carotid artery, and expired, despite arterial ligation and supportive measures.

Figure 2 shows the autopsy specimen with marked edema, reaction and deformity of the larynx. The dark areas in the illustration represent hemorrhage, but do not conceal the marked edema and deformity of the structures of the larynx.

Figure 2 shows also a photomicrograph of the section taken from the epiglottis. This shows a marked necrosis and degeneration of the elastic cartilage of the epiglottis with residual islands of tumor

Fig. 1.—Larynx of Case 1, opened from behind. Postmortem specimen. Total dosage to the larynx - 7500 roentgen units. Photomicrograph of larynx. Section through thyroid cartilage, showing cartilagenous radio-necrosis, ulceration, and remaining tumor.

interdigitated between the radiation scar. Radionecrosis of the tissues is amply illustrated.

CASE 3. M.D., a 72 year old white male, presented with the history of hoarseness for six months. Examination showed a large lesion at the base of the epiglottis and a fullness over the left ala of the thyroid cartilage. Direct laryngoscopy and biopsy revealed a poorly differentiated squamous cell carcinoma. The patient refused laryngectomy, but submitted to a tracheotomy and removal of the thyroid cartilage. At the time of operation, it was found that the carcinoma had eroded through the left ala of the thyroid cartilage and extended locally, though no glands were palpable in the neck. After the wound healed, the patient was started on x-ray therapy and was treated through three 10 by 15 cm fields; two on the lateral sides of the neck and one anterior field. A fractional dosage using 200 KV therapy, at 18 milliamps and 50 cm distance, with a screening of 0.5 cm of copper and 1 mm of aluminum, alternating fields over a period of 40 treatments delivered a tumor dosage of 6950 r to the midline. Radiation reaction in the interior of the larynx was considerable, and much necrosis and sloughing occurred. A great deal of thick, tenacious discharge was continually present. It was difficult to palpate any evidence of nodes or external lesion recurrence
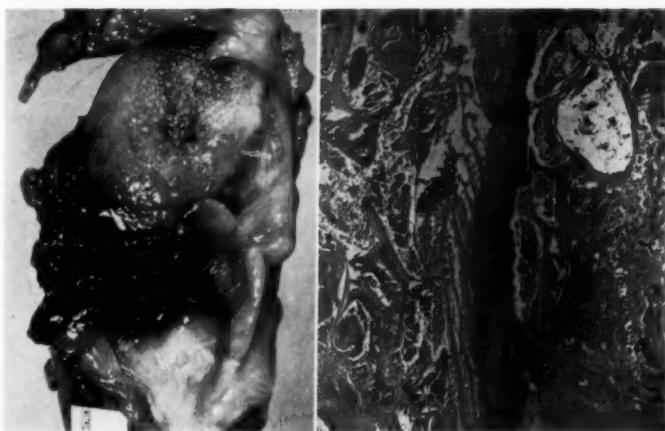
Fig. 2.—Larynx of Case 2, opened from behind. Postmortem specimen. Total dosage to the larynx - 7500 roentgen units. Photomicrograph of larynx. Section taken through epiglottis. There is necrosis and degeneration of elastic cartilage. Note islands of tumor lying in the radiation scar and the generalized radionecrosis.

locally. The patient suffered intermittently with periods of severe dyspnea caused by blocking of the airway, secondary to slough and tenacious secretion getting into the trachea beneath the No. 8 tracheal cannula. At the same time, the patient had marked dysphagia which necessitated the use of a feeding tube; he gradually lost ground until he expired six months following the termination of his radiation. Death was due to obstructive crusting of the larynx and trachea, impairing his airway and thus causing asphyxia. Autopsy revealed no evidence of extension of the lesion beyond the larynx.

Figure 3 shows the specimen obtained at autopsy, opened from behind. This illustrates the marked radionecrosis and edema of the epiglottis and anterior portions of the larynx. The photomicrograph taken of a section through the tip of the arytenoid, reveals the marked scarring, ulceration, and destructive radionecrosis with the tumor still present in the interstices of the scar tissue and a portion of the necrotic arytenoid tip still remaining.

CASE 4. E.J., a 51 year old white male, presented himself with the complaint of severe hoarseness of approximately five months' dura-
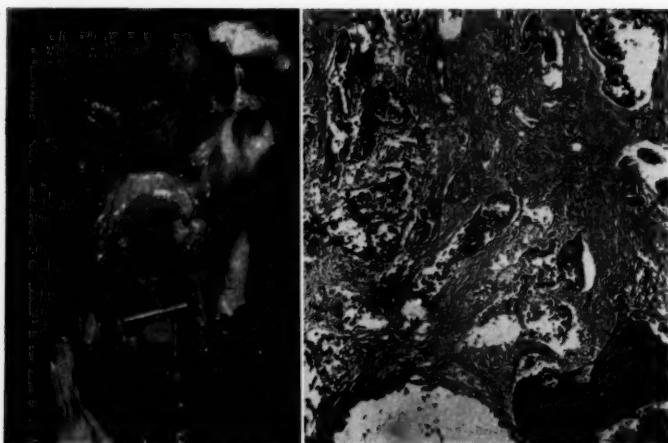
Fig. 3.—Larynx of Case 3, opened from behind. Postmortem specimen. Total dosage to the larynx - 6950 roentgen units. Photomicrograph of larynx. Section through the tip of the arytenoid. Note the marked scarring, ulceration and destructive radionecrosis. Tumor is still present within the interstices of the scar tissue.

tion.   A direct laryngoscopy and biopsy revealed a lesion of the anterior commissure extending along the left vocal cord with fixation of the left cord, but no palpable glands in the neck.   He refused laryngectomy and radiation was started using two 6 by 5 cm lateral cervical fields at 200 KV, with 18 milliamps with filters of 0.5 mm copper and 1.0 mm aluminum at 50 cm distance, given in fractional dosages of 200 r to alternated fields for a total of 4500 r to each field.   This resulted in a midline dose of approximately 7000 r delivered to the tumor.   Marked radiation reaction developed in the interior of the larynx, making necessary many direct laryngoscopies in order to examine the interior of the larynx.   A positive biopsy was obtained six months following termination of radiation.   A laryngectomy was performed.   Postoperatively, he developed sloughing and hemorrhage from the carotid area on the left, which necessitated plastic procedures with large skin flaps to cover the defect and eradicate the postoperative esophageal fistula.   The patient died of metastasis and local recurrence two years later.

Figure 4 shows the appearance of the larynx opened from behind. The lesion can be seen involving the entire left cord and anterior
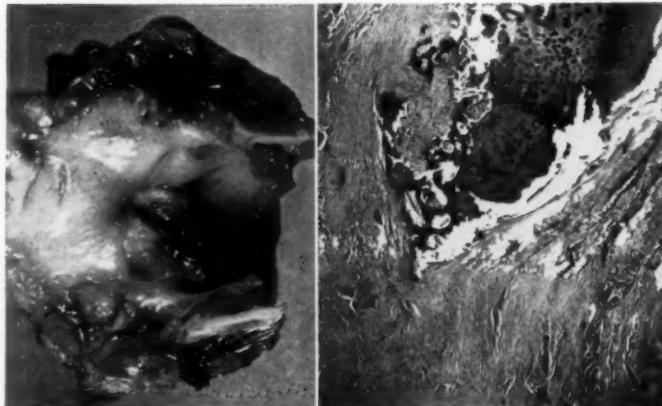
Fig. 4.—Larynx of Case 4, opened from behind. Surgical specimen. Total dosage to the larynx - 7000 roentgen units. Photomicrograph of larynx. Section through the thyroid cartilage, including part of the irradiated lesion with marked necrosis of cartilage and the usual islands of cancer in the scar tissue.

commissure, extending somewhat onto the right cord. The marked radionecrosis of the area is seen with edema of the epiglottis and anterior of the larynx being quite pronounced. The microsection is taken through the thyroid cartilage, including part of the irradiated lesion. The radionecrosis and involvement of the cartilage is illustrated with marked scarring of the tissues and tumor islands lying in the scar.

CASE 5. F.S., a 51 year old white male, presented with a history of hoarseness for approximately nine months. The patient had a lesion involving the anterior commissure, base of the epiglottis and right vocal cord, which proved to be squamous cell carcinoma. He refused laryngectomy and radiation was instituted with the same factors used in Case 4. He received 5400 r to the right field and 4500 r to the left, with a total midline dosage of approximately 7500 r. The radiation reaction was moderately severe, followed by marked deformity of the epiglottis and severe edema of the interior of the larynx. This necessitated following the patient with multiple direct laryngoscopies to determine if the lesion had disappeared. After six months, the biopsy was positive for squamous cell carcinoma in the irradiated area. A laryngectomy and right radical neck dissec-

Fig. 5.—Larynx of Case 5, opened from behind. Surgical specimen. Total dosage to the larynx - 7500 roentgen units. Photomicrograph of larynx, showing marked scarring with tumor islands lying in the scar tissue.

tion were performed six months following the termination of radiation. A large esophageal fistula resulted with breaking down of the wound and considerable bleeding from the external carotid artery. The right carotid was ligated following a severe episode of bleeding, and large skin flaps were placed over the defect to close the esophageal fistula and protect the carotid area from bleeding. The patient died eighteen months later.

Figure 5 shows the surgical specimen opened from behind displaying the marked edema and deformity of the epiglottis, and the interior of the larynx. The tumor is still not eradicated by the irradiation.

The photomicrograph of the biopsy specimen illustrates the marked scarring with tumor in the interstices of the scar tissue. The radiation obviously had not eradicated the tumor despite the heavy dosage of radiation.

COMMENT

Figure 6 shows a mirror view of a larynx that has completed a course of radiation two months prior to the picture. This amply illustrates the marked edema and distortion of the interior of the larynx which makes it difficult to follow these cases by indirect means

Fig. 6.—Mirror view of the living larynx that has completed a course
of radiation therapy two months prior to the photograph.

after radiation.   Because of this marked edema and swelling of the
interior of the larynx, frequent direct laryngoscopies and biopsies are
mandatory in following cases that have been irradiated for carcinoma
of the larynx.   It is very easy to overlook a recurrence of the tumor.
The cases illustrated also suggest that radiation in many squamous cell
lesions of the larynx is ineffective even when adequately treated by
the above commonly used method of irradiation.

To date, we have not been able to abtain specimens of larynges
that have been radiated with cobalt.   However, in the few cases that
have been seen, the reaction has been identical to that using the 200
KV therapy units, which are commonly used throughout the country
at the present time.[5]   The question of whether the cobalt and beta-
tron types of therapy will give better results than conventional ther-
apy is yet unanswered.   There is no doubt that with these newer
forms of therapy, less skin reaction and better localization of the
therapeutic effect with the more pure form of radiation and ionization
are obtained.[6-8]   But the ionizing rays are concentrated upon the
tumor, which is usually located in the interior of the larynx, so the
effect can be no different from that occurring in the above illustrated
cases, providing adequate dosage is used.   The persistence of the radio-
edema in the interior of the larynx with the chronicity of the ulcera-
tions and mucositis that prevails, and the difficulty of examining these
patients, lead us to the conclusion that radiotherapy of the larynx
in such advanced cases is not as desirable as surgery.   The destructive
effect produces poor voice, marked dysphagia, and frequently makes
tracheotomy necessary to give adequate airway.   An irradiated larynx
follows a definite pattern of redness, edema, stenotic lymphedema,
perichondritis, subperichondrial abscess, chondral necrosis, destruction

of the laryngeal cartilages, fibrosis, cicatricial contraction with deformity of the lumen, and obliteration of the lumen with chronic ulceration and sloughing of the interior of the larynx.[5,8-11]   This follows practically all adequate radiation therapy to this organ, if the lesion is extensive.   Aside from the local reaction, the voice is often severely impaired, there is pain locally, dysphonia, stridor, reflex pain, and dysphagia, which is more severe than in a clean surgical procedure.   The advantages of surgery include the better airway, freedom from the reaction of radiation, and the development of a good esophageal voice with persistent training.

The authors do not dispute that radiotherapy has taken a place in the treatment of small cord lesions in which the cancer is clearly confined to the mid-cord with that structure showing no limitation of motion on phonation.[9,12,13]   But they do feel that in more advanced lesions, the only place for radiation therapy is in palliation for inoperable, far advanced cases, and will continue to feel this way unless great improvement in radiation technique is forthcoming in the future.

SUMMARY AND CONCLUSIONS

1. A cancerocidal dose of irradiation invariably leaves a residual effect in the larynx which is persistent.

2. Five cases have been shown where actual laryngeal specimens have been obtained illustrating the marked reaction of radiation on the interior of the larynx.

3. Because of the severe edema, it is impossible to follow these patients without doing many direct laryngoscopies and biopsies to determine the effect of the treatment by irradiation.

4. Subsequent surgery on cases that have been irradiated is made much more difficult and dangerous, due to the marked loss of healing power of the tissues.

5. The authors believe that at the present time, radiation for extrinsic carcinoma of the larynx should be confined to treatment of patients who absolutely refuse surgery, and as a palliative measure only.

6. Irradiation therapy with the present techniques does not take the place of surgery in extrinsic carcinoma of the larynx.

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IX

TETRACAINE ANESTHESIA IN ENDOSCOPY

AN EVALUATION

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According to Knudsen and his co-workers,[9] the demands to be made on an ideal method of anesthesia for endoscopy are: 1) a minimum of risk to the patient, 2) removal of discomfort to the patient, 3) undisturbed working conditions for the surgeon, 4) simplicity of technique and apparatus, an 5) a short restoration period. There have been numerous articles in the literature extolling various drugs for this purpose, but the majority, after enjoying a brief popularity, are employed less and less.

General anesthesia has the advantage of affording oblivion to the patient during the procedure and gives the endoscopist the maximum amount of relaxation. This method has the disadvantages of removing the cough reflex, which is a great aid in obtaining secretions, and there is the period of unconsciousness afterwards. Schoemperlen[13] employed this method in over 4000 cases, but warns of the danger of pentothal and curare in asthmatics.

Topical anesthesia seems to be preferred by the majority of broncho-esophagologists. Cocaine was the first drug employed for this purpose and is used still by quite a few surgeons. McKinney[10] found that it gave excellent anesthesia by the transtracheal route, but this method is not without danger and complications. Cocaine produces cardiac reactions which are not as readily amenable to resuscitation as the nervous and respiratory reactions of the newer synthetic topical anesthetics. Hughes et al[6] reported excellent results with Dyclone,® but a large amount of the drug was used, even though they had no untoward reactions. Of the newer drugs, tetracaine seems to enjoy the most popularity. Kleits[8] found that 0.5% tetracaine alone was totally incompetent to produce satisfactory topical

anesthesia for peroral endoscopy and used a 2% solution of tripelennamine with this drug. Hulse[7] used 1% tetracaine and obtained satisfactory anesthesia but found that 2% tripelennamine along with the tetracaine gave an anesthesia that was inferior to tetracaine alone. Many authors have reported potentiating topical anesthesia with tetracaine by using a "lytic cocktail" of promethazine and diethazine along with meperidine[2,3,5,11] and Wyant and his co-workers[14] used these and a curare-like agent to give greater relaxation. Altman and Fialkow[1] used meperidine intravenously with topical tetracaine and found that less of the local anesthetic solution was used, but Bolstead and Ditzler[4] recommend that, because of the marked depression which these drugs produce, the potentiating drugs be used only when topical anesthesia alone appears to be inadequate.

In this hospital I have employed 0.5% tetracaine alone in over 3900 endoscopic procedures (Table I). The patients are given 0.1 gm sodium pentobarbital one hour prior to the procedure, followed by .002 gm of dilaudid and either 0.3 or 0.4 mgm of scopolamine one-half hour before being taken to the operating room. In asthmatics and debilitated patients, the dilaudid and scopolamine are omitted and Demerol,® 50 mgm, is substituted. The patients for bronchography receive sodium pentobarbital as above and codein 0.6 gm and atropine 0.4 mgm. In the operating room the pharynx is sprayed twice at a three minute interval with 0.5% tetracaine containing 1:15000 epinephrine using an average of 1.0 cc of solution for this. Then four instillations of this solution are made into the larynx and trachea using a syringe and cannula. These are in 1 cc aliquots and are given five minutes apart. For direct laryngoscopy and esophagoscopy, only the spray method is used, being administered four times at five minute intervals and using a total of 2.0 cc of solution.

No reactions have been encountered in any of these cases and in only 12 was bronchoscopy unsuccessful at the first attempt. In four of these a second bronchoscopy was without incident and in the other eight, general anesthesia had to be employed. These latter patients had small mouths and short necks and needed the additional relaxation afforded by general anesthesia. None of the patients with pulmonary tuberculosis showed any unfavorable influence on the disease. We have not noticed any toxic effects in asthmatics as other workers have mentioned.[12] In all cases the cough reflex returned in not more than an hour and the patients were fully awake. It is believed that this is due to the comparatively small amounts of pre-anesthetic medication and the small amounts of tetracaine which were used.

TABLE I

PROCEDURE	NO. OF PATIENTS	NO. OF PROCEDURES
Bronchoscopies		
Pulmonary Tuberculosis	1020	2093
Non-tuberculous	378	581
Asthma, Bronchial	25	48
Bronchiectasis	118	313
Direct Laryngoscopies	34	56
Esophagoscopies	29	52
Bronchographies		
Pulmonary Tuberculosis	293	431
Non-tuberculous	255	417

SUMMARY

1. The use of tetracaine 0.5% solution for topical anesthesia in over 3900 endoscopies has been presented.

2. There have been no reactions at the time of anesthesia and very few unsuccessful procedures.

3. No untoward reactions have occurred following endoscopy.

4. It is felt that 0.5% tetracaine provides safe and adequate anesthesia for all endoscopic procedures.

CONCLUSION

It is felt that using 5 cc tetracaine in an 0.5% solution with 1:15000 epinephrine and a moderate amount of premedication in our hands gives most satisfactory anesthesia for peroral endoscopic procedures. In only a very few instances will general anesthesia have to be employed and this will be because of anatomic conditions. The use of potentiating drugs has the disadvantage of prolonging the

effects of the anesthetic and this is undesirable in pulmonary conditions, since early return of the cough reflex is necessary.

VETERANS' HOSPITAL

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X

THE OTOTOXICITY OF KANAMYCIN
IN GUINEA PIGS

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Shortly after the introduction of kanamycin reports of the various side effects began to make their appearance in the literature. A number of clinical cases of auditory and vestibular toxicity in humans have been reported.[1-5] Severe renal, auditory and vestibular damage has occurred in tuberculosis cases treated for long periods of time with kanamycin.[6-9] Other authors have reported little or no ototoxicity following the short term use of this drug.[10,11]

Kanamycin was discovered by Umezawa.[12] It was produced from a new species of bacteria designated by the name Streptomycetes kanamyceticus and resembles neomycin in its structural formula. Both antibiotics have a deoxystreptamine moiety but they differ in the two amino sugars that are glucosidically linked. The structural formula has been worked out by Cron et al.[13] This promising antibiotic has been shown to be active in vitro against many Gram-positive, Gram-negative and acid fast organisms while appearing to be relatively inactive against clostridium, diplococci, and streptococci.[14-16] The pharmacological action of kanamycin is considered to be bacteriocidal. Thus far it has been very useful in the treatment of drug resistant staphylococcal infections.[3,5,11]

Clinical and laboratory studies suggest that kanamycin is less toxic to the vestibular system than streptomycin and far less toxic to the auditory system than either dihydrostreptomycin or neomycin.[3,5;10,11] This was demonstrated by Hawkins[17] who gave kanamycin to cats, rats and guinea pigs. A comparative study revealed

that toxic symptoms appear much earlier in cats given streptomycin and dihydrostreptomycin than in those given equivalent doses of kanamycin. The severe damage to the outer hair cells of the organ of Corti in cats given toxic doses of kanamycin was demonstrated. Some degeneration of the nerve fibers and ganglion cells was present in those receiving very high toxic doses. The cochlear potentials were diminished or absent. Rats appeared to be less susceptible to the toxic effects of kanamycin. Large doses resulted in selective damage to the nerve and ganglion cells. In guinea pigs severe outer hair cell damage with sparing of the inner hair cells was seen. The nerve and ganglion cells were normal. Cochlear potentials had not been tested in guinea pigs at that time.

The purpose of this experiment was to determine the toxic effects of kanamycin on the peripheral auditory and vestibular system and the central nervous system, of guinea pigs. It was believed that correlation of observations of vestibular and auditory function with the histopathological findings would give a more clear understanding of the toxic effects of kanamycin.

<div align="center">METHOD</div>

These experiments were carried out on 29 young healthy guinea pigs. They were given daily intramuscular injections of kanamycin of varying dosage (30 to 800 mg/kg of body weight) for varying periods of time (5 to 30 days). Daily observation of general health, weight and of the presence or absence of the Preyer pinna reflex were made. Every three days during the acute toxicity period, the righting reflex, positional, optokinetic and postrotatory nystagmus were tested. Postrotatory tests were later dispensed with upon recognition that habituation takes place rapidly in normal guinea pigs. Observations of the changes in daily weight, over all health and behavior proved to be the best indications of the severity of general toxicity. After discontinuance of the drug the guinea pigs were kept for intervals of time varying from 1 to 150 days. Prior to sacrificing for histological examination the cochlear potentials were recorded.

The animals were anesthetized with Dyallilbarbituric acid with ethyl carbamate (0.5 mg/kg of body weight) given intraperitoneally. The surgical procedure for implanting differential electrodes in the basal turn of the cochlea and for recording of cochlear potentials to sound stimuli have been described elsewhere.[18]

The 19 guinea pigs surviving completion of the experiment had their temporal bones fixed by intravital fixation with Heidenhain-

Susa solution according to the technique described by Schuknecht.[19]
Both temporal bones, brain stem, cerebellum and a portion of the
cerebral crotex were removed en bloc and immersed in fixative. After
processing the specimens were serially sectioned in 16 μ thicknesses
in a horizontal plane, and every tenth section was stained by routine
technique with hematoxylin-eosin. These sections were thoroughly
studied microscopically for any pathological changes. The temporal
bone of a representative specimen was graphically reconstructed and
charted (Figs. 2, 3) in the manner described by Guild[20] and modified
by Schuknecht.[19]

<div align="center">RESULTS</div>

Thirteen of the 16 guinea pigs that received 200 mg/kg or less
for 10 to 30 days survived completion of the experiment. Three of
this group died of other causes and were discarded. Tests of auditory
and vestibular function, general behavior and histologic examination
of sections of the temporal bones, brain stem, cortex and cerebellum
revealed no abnormalities.

The 13 guinea pigs receiving 800 mg/kg of kanamycin daily
for five days all showed severe toxicity. These symptoms appeared
soon after the first or second injection. They were manifested by
listlessness, diminished general activity, refusal to eat, failure to gain
weight or weight loss and falling out of hair. By the fourth to fifth
day some animals would lose consciousness about one to two hours
after the injections but showed partial recovery by the following
morning. Seven of this group died of severe toxicity between the
sixth to eighth days and were discarded. The pinna reflexes in all
animals of this toxic group were markedly depressed to totally absent
by the third to sixth day. They showed a moderate to severe ataxia
and disequilibrium, staggering, falling and sometimes circular motion.
When they were allowed to survive after the severe toxicity some
compensation with diminution in these symptoms would occur. Dis-
tinct loss of righting reflex was observed only in two guinea pigs.

Cochlear Function. Thresholds and maximum output of coch-
lear microphonics and action potentials in twelve out of the thirteen
"non-toxic" animals were considered within normal limits. Record-
ings were not made in one of these animals because of the presence
of otitis media.

The potentials were recorded in five of the six toxic animals
surviving completion of the experiment. In one animal accidental

TABLE I

ANIMAL NO.	COCHLEAR MICROPHONICS Thresholds in db*							NERVE ACTION POTENTIAL Threshold in db*		
	125 cps	250 cps	500 cps	1000 cps	2000 cps	4000 cps	8000 cps	2000 cps	4000 cps	8000 cps
NON-TOXIC MEAN **	50	66	73	83	73	82	77	68	72	68
A-592	0	0	0	0	0	20	29	0	18	20
A-635	26	39	60	67	57	69	68	45	57	54
A-658	0	0	19	36	23	24	36	34	35	24
A-684	0	14	44	40	46	48	36	39	27	21
A-686	0	0	9	10	4	13	0	10	5	0

* Cochlear microphonics and action potential thresholds as measured on the dials of the attenuator.

** Non-toxic mean compiled from average of recordings of the 12 non-toxic animals. 0 db indicates no response seen at the maximum of the stimulus at that frequency.

injury to the tympanic membrane during operation terminated attempts to record the cochlear responses. Increase in thresholds of microphonics and action potentials in the toxic animals are presented in Table I. Also there was considerable decrease in the maximum output of the responses as compared with standard measurements in our laboratroy. At some frequencies there was total absence of response at the maximum intensity. The greatest loss of cochlear function was present in guinea pig A-592. Histopathologic changes in this specimen wer. only moderately severe compared to animal A-658 (Fig. 1) in which the thresholds are not as markedly increased. It was apparent that direct correlation of threshold shifts with degree of histopathology could not be made in this experiment.

Histologic Findings. One specimen of the six toxic animals surviving completion of the experiment was misplaced during processing. The histologic sections of the other five had a similar pattern of degenerative changes in the peripheral organs. The striking feature
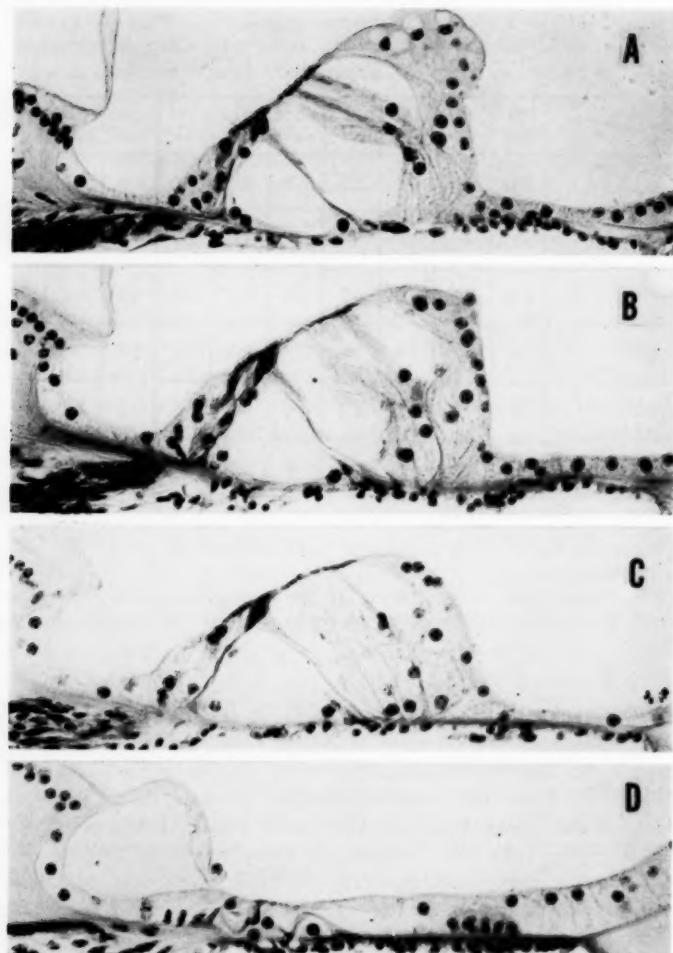
Fig. 1.—Guinea pig A-658. Photomicrographs of Corti's organ at 18.5 mm (A), 15.4 mm (B), 11.4 mm (C), and 5.9 mm (D). This animal received 800 mg/kg of kanamycin for five days. Intravital fixation was carried out on the 15th day. H-E, X275.

HAIR CELL DAMAGE

• NONE

25%

50%

100%
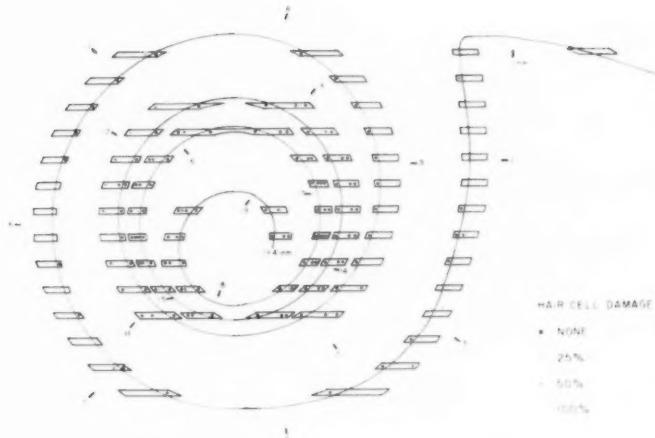
Fig. 2.—Guinea pig A-658. Graphic reconstruction of the organ of Corti showing severe outer hair cell destruction with spotty inner hair cell damage.

was the severe selective destruction of the outer hair cells especially in the basal turn. Outer hair cell damage in the third and apical turns was less severe (Fig. 1). Some spotty loss of inner hair cells was seen in the basal turn (Figs. 1, 2). The damage to the supporting cells closely paralleled the hair cell destruction and is clearly illustrated in Figures 1 and 3. These changes were prominent in the Deiter's cells which showed complete atrophy in some sections and in others were partially collapsed with their degenerated nuclei resting on the basilar membrane. Some sections had degenerative changes in the outer sulcus cells with diminution in cell numbers. Isolated areas of the limbus spiralis had complete loss of celluarity except for the Huschke's cells. No abnormalities were seen in the scalae, Reissner's membrane, tectorial membrane, strial vascularis, spiral ligament or the basilar membrane. A definite decrease in the gangion cells and nerve fibers of the VIII nerve was present in one of toxic specimens.

No distinct pathological changes of the peripheral vestibular receptors were observed by ordinary light microscopy. In a few sections there was questionable diminution of the number of sensory cells with some slight flattening of the maculae of the sacculus and utriculus.
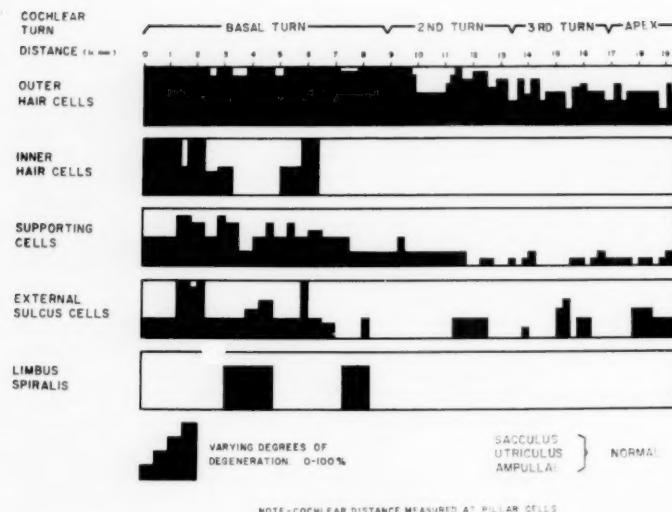
Fig. 3.—Cochlear chart of guinea pig A-658.   Observe the parallel damage to the outer hair cells and supporting cells.

Hematoxylin-eosin and special stains (Klüvers stain) revealed abnormalities of the central nervous system in three of the nineteen specimens.   These consisted of patchy, disseminated, rarified areas primarily involving the granular layers in the cerebellum (Fig. 4). Spotty light staining areas in the brain stem suggested degeneration of ground substance with sparing of the cellular elements.

COMMENT

The histopathology in the cochlea of guinea pigs given toxic doses of kanamycin was similar to that described by Hawkins.[17]   The initial effect of the drug appeared to be on the outer hair cells and supporting cells of Corti's organ.   These changes were compatible with the marked threshold shifts of cochlear microphonics and actions potential output to sound stimuli for the various frequencies tested. But direct correlation between function and histopathology could not be made.   No abnormalities were seen in the peripheral vestibular system.

Fig. 4.—Guinea pig A-684. Patchy, disseminated, rarified areas involving primarily the granular layer of the cerebellum. Klüvers stain, X55.

Kanamycin, neomycin, streptomycin, and dihydrostreptomycin belong to the family of antibiotics produced from the genus Streptomycetes. The primary site of damage to the auditory and vestibular systems by these drugs has been a controversial subject for many years. Damage to the peripheral receptor organs by streptomycin and dihydrostreptomycin has been demonstrated in animal experiments.[21-23] Central nervous system pathology has also been obtained in animals given toxic quantities of these drugs.[24-26] The persistence of this controversy may stem from failure to examine serial sections of both the peripheral receptors and the central nervous system of all specimens.

Severe ataxia or disequilibrium or both was observed in the toxic guinea pigs. In the absence of abnormalities in the peripheral vestibular receptors these symptoms can be explained by the distinct degenerative lesions in the central nervous system. Patchy, disseminated, rarified areas in the granular layers of the cerebellum and spotty light staining areas (suggestive of degeneration of ground substance) in the brain stem have not been previously described in guinea pigs given toxic quantities of kanamycin.

Renal, auditory and vestibular toxicity in clinical cases have been reported.[1-5] A compromised renal function appeared to predispose to toxicity following even relatively small amounts of this drug.[1,2]

Prolonged use of kanamycin as required in the treatment of tuberculosis also carries the potential hazard of toxicity.[6-9]   In humans the initial toxic symptoms were usually tinnitus and loss of hearing followed by vertigo with disturbances of equilibrium.   Discontinuance of the drug upon the appearance of any threshold shift has resulted in recovery or stabilization of symptoms in some cases.[6]   Kanamycin has given great promise as a valuable antibiotic for the treatment of drug resistant infections.   In view of the potential toxicity to the renal, auditory, vestibular and central nervous systems, use of this drug should be reserved for selected cases.   Frequent audiometric examination is suggested as the best method for detecting early auditory toxicity.

The selective destruction by kanamycin of the outer hair cells in guinea pigs may be a valuable tool in further studying the interrelations among the various cochlear potentials.   Further experiments on the effect of this drug on cochlear function are in progress in our laboratory.

SUMMARY

Guneia pigs given toxic quantities of kanamycin manifested general toxicity, severe ataxia or disequilibrium or both with staggering and falling.   These animals had loss of hearing confirmed by marked threshold shifts in cochlear microphonics and action potentials. The patterns of histopathological changes in all specimens of the toxic animals were similar.   There was severe damage to the outer hair cells and supporting cells with relative sparing of the inner hair cells.   The vestibular receptors were considered normal.   One specimen had diminution in the VIII nerve fibers and ganglion cells.   Three of the toxic animals showed patchy, disseminated, rarified areas primarily involving the granular layers of the cerebellum.   Spotty, light staining areas believed to indicate degeneration of ground substance with preservation of cellular structure were present in the brain stem.

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XI

THE EFFECTS OF CHLORPROMAZINE
UPON THE EAR AND THE
VIII CRANIAL NERVE

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In the past, afferent neural impulses transmitted by specific path-
ways were thought to be neither facilitated nor inhibited during their
course from the peripheral sense organ to the cerebral cortex. Recent
studies, however, indicate that sensory impulses may be regulated and
controlled at many neural levels between the receptor and the cor-
tex.[7,23,29] Moreover, it has been shown that neural response patterns
evoked by stimulation can be modified by experience and training.[18,19]

Granit and Kaada[11] discovered that the activity of the muscle
spindle, an important kinesthetic receptor, could be modified by stim-
ulation of neurons in the central nervous system. This control was
exercised by activating or suppressing the small motor horn cells which
had already been shown to govern the rate of discharge of spindle
afferents. The muscle spindle afferents could be "driven" faster or
slower or stopped altogether by stimulating either facilitory or inhibit-
ory centers with implanted electrodes.

Potentials evoked by visual stimuli and recorded from the optic
tract, lateral geniculate body, and striate cortex have been reduced in
magnitude or abolished altogether when cats were presented with an
acoustic or olfactory stimulus.[17] This reduction in magnitude of the
visually evoked potential occurred both within the specific sensory
pathways and in the midbrain reticular formation. Since the reduc-
tion was evident within the optic tract, the blocking effect was assumed
by the experimenters to have occurred at the retinal level.

Galambos,[7] recording from the round window membrane of the
cochlea of the cat, demonstrated inhibition in the auditory nerve dis-

charge (N_1) by electrical stimulation of the floor of the medulla. Shock stimulation was applied to the medulla at the site of the olivo-cochlear pathway, a collection of fibers that originate in the superior olivary region and terminate near or on the inner hair cells of the contralateral cochlea. The preparations all showed that N_1 was not affected until one to four shocks had been applied to the medulla. The acoustic stimulus was a click near threshold for a nerve response from the ear. Shock to the medulla completely obliterated the N_1 response when the acoustic stimulus was a click approximately 15 db above established threshold intensity; whereas, the shock to the medulla reduced the N_1 response by about 40 per cent when the acoustic stimulus was a more intense click (35 db). The phenomenon persisted after removal of the muscles of the middle ear, but it disappeared when the olivo-cochlear bundle was severed peripheral to the site of stimulation. Galambos concluded that the nerve impulses aroused in the medulla by electrical stimulation pass out to the cochlea where they suppress the response of the first-order neurons of the auditory nerve. According to Galambos, it is possible that the efferent fibers prevent conduction at the point where they wrap around the afferent fibers. It is also possible that the efferent fibers which pass directly to the hair cells may create conditions unfavorable for the arousal of auditory nerve impulses.

Inhibition in the auditory system has also been demonstrated by Hernandez-Peon, Scherrer, and Jouvet.[19] While recording nerve responses from the dorsal cochlear nucleus of a cat to auditory clicks, they found that the specific evoked potentials were practically abolished when a visual stimulus (two mice in a bottle) elicited behavioral evidence of attention from the cat. When the mice were removed, the auditory responses returned to the same order of magnitude. The experimenters suggested that the blocking of afferent impulses in the lower portions of the afferent pathways may be involved in limiting the scope of attention. Apparently, afferent activity may be markedly reduced while still in its trajectory toward higher levels of the central nervous system.

In the frog, Löwenstein[24] showed that the number of impulses in an afferent nerve mediating touch was reduced by artificial electrical stimulation of efferent sympathetic nerves to the skin region under stimulation. Since there are sympathetic efferent fibers involved in touch sensibility, it seems reasonable that other sensory systems might also undergo a similar form of afferent modulation.

There is evidence now that at least five of the cranial nerves (III, VII, IX, X, and XI) contain sympathetic efferent fibers. Three of

these may be important to afferent modulation in vision and taste. These efferent fibers project from the hypothalamus posteriorly and caudally to the brain stem, some as far as the medulla.[8] Further evidence indicates that there may be similar fibers in the auditory system. Rasmussen[27] described efferent fibers rising from cells near the superior olive and ascending to the floor of the medulla. These decussate, pass out the contralateral internal auditory meatus, form the vestibulo-cochlear anastomosis (bundle of Boettcher, Oort), and enter the spiral ganglion. They account for 40 to 50 per cent of the internal spiral bundle of the cochlea, and are distributed along the entire length of that organ, possibly ending at the internal hair cells. As previously mentioned, these fibers can produce inhibition of N_1 responses as evidenced by recording from the round window membrane.[7]

SENSORY INHIBITION BY DRUG ADMINISTRATION

There is evidence, too, of sensory inhibition under conditions of systemic drug administration. Chlorpromazine (3-dimethyl-amino-propyl-2-chlorphenothiazine-hydrochloride), an autonomic suppressant, apparently produces inhibition of the auditory system. This drug has been found particularly effective in reducing auditory hallucinations both in the mentally ill and in instances of experimentally induced hallucinations by the action of d-lysergic acid diethylamide, an excitant drug. Little evidence exists, however, concerning the effects of chlorpromazine on specific sensory receptors. It has been suggested by Bradley[1] that chlorpromazine produces auditory dampening somewhere in the afferent system distal to the reticular formation.

A review of the literature on treatment with phenothiazine derivatives (especially chlorpromazine) reveals frequent mention of auditory inhibition. Toll[31] reports that auditory hallucinations cease, and also that there occurs a temporary fading of voices in the surrounding environment. The effect is reported to have lasted for several hours.

In addition to clinical evidence, various experimenters have been concerned with the indifference of animals under the effects of chlorpromazine, and with the apparent sensory dampening to auditory stimuli in conditioning studies. Schneider[30] postulated that chlorpromazine has a differential influence on various sensory afferent fibers since it blocks arousal to auditory stimuli but not to painful stimuli. The observation of Fellows and Cook[6] on the blocking of conditioned responses in rats is in accord with Schneider's hypothesis. Although unresponsive to a buzzer, the rats were still capable of responding to painful shock following treatment with chlorpromazine (4.4 mg/kg).

Gleidman and Gantt[10] studied the effects of chlorpromazine on orienting behavior and retention of conditioned responses in dogs. The orienting response made to novel sounds was abolished by the administration of the drug.   Moreover, the number of conditioned paw withdrawal responses was decreased.

Courvoisier, Fournel, Ducrot, Kolsku, and Koetschet[4] found that as little as 0.5 mg/kg of chlorpromazine reduced the frequency of a response of rats conditioned to an auditory stimulus.   Higher doses abolished it.   The avoidance response to shock, however, was maintained.

In rats trained to obtain food by jumping through a hole in a partition at the sound of a buzzer, chlorpromazine (2-9 mg/kg) markedly decreased the proportion of responses without interfering greatly with spontaneous activity.[13]

Grenell[12] noted that in rats injected with chlorpromazine, environmental stimuli no longer evoked the customary responses.   The character of their state suggested an indifference to stimuli coming into the central nervous system.   The question may be raised, however, as to whether or not the results noted by Grenell might be due to a direct effect by the drug upon receptors.

THE LOCUS OF AFFERENT MODULATION

Several experimenters have attempted to locate the source of auditory dampening due to chlorpromazine.   The effects of the drug on the auditory cortex, thalamic nuclei, and the reticular formation have been studied.

Hendley, Lynes, and Berger[16] recording from the thalamus and other sub-cortical areas, tested the effects of various sounds upon arousal.   The results indicated that chlorpromazine, at high dose levels, reduced auditory responses in cat preparations as measured with thalamic electrode implantation.

Killam and Killam[21] stimulated the reticular formation and nonspecific nuclei in cats after administration of chlorpromazine (5 mg/ kg).   The drug raised the threshold for EEG arousal following thalamic stimulation from 4 to 5 volts and markedly elevated the threshold for behavioral arousal from 6 to above 13 volts.   These experimenters concluded that the drug had an inhibiting influence upon the reticular formation.

In another experiment, Killam and Killam[22] studied the drug sensitivity of the reticular formation. Potentials were recorded from the dorsal cochlear nucleus and medial geniculate body following a click stimulus to the ear. When an 8 volt shock was applied to the reticular formation, there was some depression of the cochlear response, but little effect was noted on the geniculate body. At 10 volts, both responses appeared to be depressed. Following chlorpromazine (1 mg/kg) a 6 volt shock to the reticular formation was now sufficient to inhibit responses from both the cochlear nucleus and the geniculate body. The authors concluded that the ability of the reticular formation to inhibit the auditory system was enhanced by chlorpromazine.

The results of Bradley[1] do not agree with those of Killam and Killam concerning the locus of dampening. Bradley studied the effects of chlorpromazine in the conscious and unconscious cat. In the conscious animal, the main effect of chlorpromazine was to induce a state of indifference indicated by failure of the animal to give a behavioral response to auditory, tactile, or visual stimuli. When similar doses (2-4 mg/kg) were administered to anesthetized cat preparations, Bradley found that stimuli (auditory or tactile) were no longer effective in producing behavioral arousal (opening of the eyes, contraction of the nictitating membrane) even in preparations which previously were easily aroused by such stimuli. Moreover, changes of the electrocorticogram, ordinarily indicating arousal, could no longer be obtained to auditory stimuli. When Bradley studied the action of the drug on the reticular formation, there was partial inhibition of arousal to afferent stimulation. He concluded that the depressive action of the drug on the reticular formation was very slight and may have been due to the drug action on the receptors related to the afferent collaterals entering the reticular formation at the brain stem and mesencephalic levels.

PURPOSE OF THE PRESENT EXPERIMENT

There seems to be little doubt that the function of the peripheral sense organ can be modified in its generation of impulses within the first-order neurons. Galambos has demonstrated inhibition in the cochlea, Hernandez-Peon at the retina, Granit and Kaada in the muscle spindle, and Löwenstein at the touch receptor.

There also appears to be little doubt that chlorpromazine affects the sensitivity of sensory mechanisms as measured by behavioral or physiological criteria. The clinical evidence and the conditioning studies already cited strongly indicate dampening in the auditory sys-
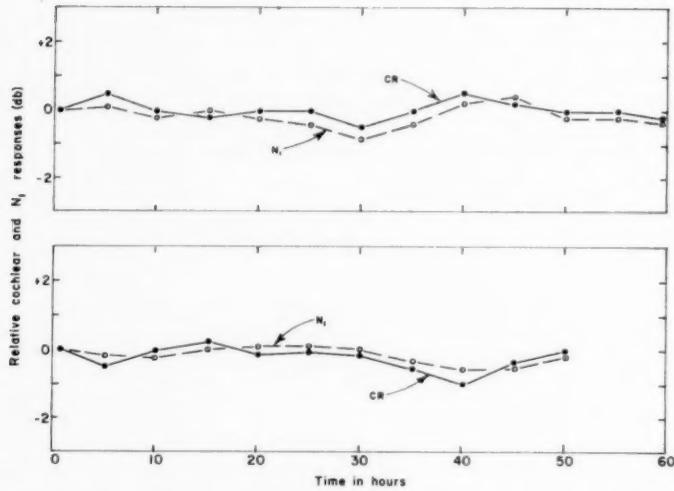
Fig. 1.—Cochlear (solid line) and N₁ (dashed line) responses obtained from each of two guinea pigs representative of Control Group I. The stimulus was an acoustic click. Both responses are given in decibels relative to response magnitudes at the stimulus reference intensity at the beginning of the experiment. Body temperature was held constant ($\pm 1°$) at $37°$ C, and no chlorpromazine was administered.

tem due to the action of this drug. However, there is disagreement as to the location of the dampening mechanism. Killam and Killam place the locus at the reticular formation, and Bradley postulates some point in the afferent system distal to the reticular formation.

In view of the evidence cited, the purpose of the present experiment was to investigate the effects of chlorpromazine on the peripheral auditory receptor and the first-order neurons of the VIII cranial nerve.

METHOD

Eleven adult guinea pigs were used as experimental and control animals. Their weights ranged from 400 to 700 grams, and their daily diet consisted of about 35 grams of rabbit chow (Purina) and a plentiful supply of fresh greens. Water was always available.

Anesthesia. Anesthesia was produced with ethyl carbamate (Urethan, U.S.P., Merck) in 20 per cent aqueous solution (pH=6.0).

The anesthetic was injected intraperitoneally in a dosage of 11 cc per kilogram of body weight. The drug in this dosage produced a surgical level of anesthesia within one hour and maintained the preparation in good physiological condition for the duration of the experiment. Because the animals were agitated at the time of anesthetization, the anesthetic was administered in two equal parts separated by approximately 30 minutes.

In three animals the anesthetic caused respiration to become depressed. To prevent respiratory failure, 0.5 cc nikethamide (Coramine®) in 25 per cent aqueous solution was injected intraperitoneally.

Surgical Procedure. The tympanic bulla was approached laterally through a 1 cm incision in the skin posterior to the pinna. Dissection was begun from a point 1 cm dorsal to the posterior tip of the mandible. This entry gave access to a part of the mastoid portion of the temporal bone anterior to the lambdoidal ridge. After removal of the periosteum, a hole (diameter 1 mm) was drilled with a small burr until the middle ear cavity was reached. The bone in this region is about 0.5 mm thick. The proper place of drilling was midway between the lambdoidal ridge and the external auditory meatus. The opening was enlarged until the round window membrane was accessible for placement of a recording electrode.

Method of Stimulation and Recording. Two different stimuli were used in this experiment. When the cochlear potential was under investigation, the stimulus consisted of a 1000 cycle pure tone. When N_1 (VIII nerve response) was under study the stimulus consisted of an acoustic click.

An audio oscillator (Hewlett Packard, 200 AB) was used to produce the tonal stimulus. The signal from the oscillator fed into an attenuator (Hewlett Packard, 350 B) with a range of 110 db, variable in steps of 1 db. The output from the attenuator led directly to a 12 cm cone loudspeaker housed in a soundproof chamber. Aerial sound was conducted from the speaker into the external meatus through a tube. A cannula at one end of the tube was sealed within the external meatus so that the tip of the cannula was approximately 4 mm from the tympanic membrane.

The acoustic click was generated by driving the same loudspeaker with a six-volt D.C. current. A click occurred on both "make" and "break." The spectrum analyses on both "make" and "break" were
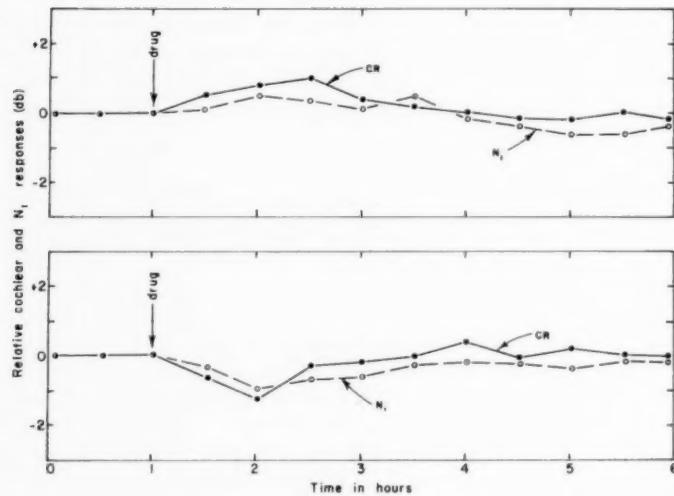
Fig. 2.—Cochlear (solid line) and N₁ (dashed line) responses obtained from the two guinea pigs in Experimental Group I. The stimulus was an acoustic click. Both responses are given in decibels relative to response magnitude at the stimulus reference intensity at the beginning of the experiment (prior to chlorpromazine administration). Body temperature was held constant ($\pm 1°$) at $37°$ C. Chlorpromazine (5 mg/kg) was injected intraperitoneally.

about the same. Aerial sound was conducted to the ear in the same manner as already indicated.

The active electrode was a piece of platinum foil (2.5 micra thick) cut in the form of an isosceles triangle 1 mm wide at the base and 2 mm high. The base of the electrode was soldered to the end of a copper wire enveloped in nylon. An inactive electrode made from a steel hypodermic needle was inserted into exposed tissue surrounding the incision.

The tip of the recording electrode was placed upon the niche of the round window by means of a micromanipulator. The cochlear and N_1 responses picked up with the active electrode were amplified and measured with an audio frequency spectrometer (Brüel and Kjaer, type 2109). The cochlear potential obtained to the 1000 cycle tone was fed directly to the output meter of the audio-spectrometer. The

cochlear and N_1 responses obtained to the acoustic click were fed into the recording attachment of the spectrometer (Brüel and Kjaer, type 2304).

<center>PROCEDURE</center>

The anesthetized animal was shaved with an electric clipper in the head region. Thereafter the incision was made and the auditory bulla exposed. The bone was drilled to give access to the round window membrane. Then the cannula on the sound tube was inserted and sealed within the external meatus. A tight seal was effected by wrapping the pinna around the cannula and taping it closed with plastic tape. During the experiment, each animal was isolated in an electrically shielded room.

The body temperature of the preparations was measured with a laboratory thermometer placed under the side of the animal as he lay on the operating table. Generally it was necessary to raise body temperature to normal (37°) before beginning the experiment since it tended to fall slightly below normal during experimental preparations as a result of anesthesia.

At normal body temperature, control data were obtained on each animal. These data consisted of an intensity function (cochlear output as a function of the intensity of a 1000 cycle stimulus), cochlear potential measures to a constant stimulus over a period of 30 to 60 minutes, and cochlear and N_1 responses produced by the click at a constant intensity. The click stimulus was administered every ten minutes during this control period. The attenuator was adjusted so that a cochlear response of 30 microvolts could be read at the output meter for the 1000 cycle tone and this intensity was used throughout the experiment.

The initial measures of the cochlear and N_1 responses were taken in order to measure normal fluctuations. Thereafter, experimental animals were injected with chlorpromazine intraperitoneally in a dosage of 5.0 mg/kg. The 1000 cycle stimulus was administered continuously throughout the experiment, except for brief intervals during which a series of six click stimuli were administered. The series of clicks was given every ten minutes. This procedure was continued until the animal expired, or the experiment was terminated.

In order to determine the extent of fluctuation in cochlear and N_1 responses, each of four anesthetized animals was maintained at
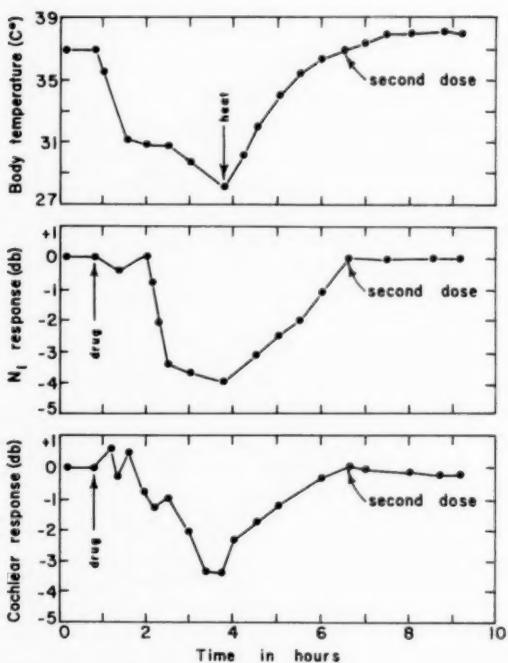
Fig. 3.—Cochlear and N1 responses obtained to an acoustic click on a guinea pig in Experimental Group II. Responses are given in decibels relative to response magnitudes prior to chlorpromazine administration. The intensity of the click was constant. Body temperature was not held constant and is reported in degrees, C.

normal body temperature ($37°$ C $\pm$ $1°$) and no chlorpromazine was administered (Control Group I). Two other animals were used to study the effects of chlorpromazine upon body temperature in unanesthetized animals (Control Group II).

In order to determine the effects of chlorpromazine upon the ear and the VIII nerve, this drug was administered to each of five anesthetized preparations. Body temperature was held constant at the normal level in two animals (Experimental Group I) but in the remaining three preparations (Experimental Group II) hypothermia was allowed to occur.

Regardless of treatment, all experimental and control animals were maintained under conditions of constant room temperature (22° C ± 1°).

Analysis of Cochlear and N_1 Responses. The cochlear and N_1 responses to the click recorded from the round window were amplified and recorded on paper by the level recorder attachment of the spectrometer. Using noise level as the reference (0 db), the magnitudes of both the cochlear and N_1 responses could be read directly from the tracing in decibels. The latency of the N_1 response was measured in milliseconds.

<div align="center">RESULTS</div>

Data gathered in this experiment indicate that under certain conditions chlorpromazine in doses of 5.0 mg per kilogram of body weight affects the magnitude of the cochlear response and the compound potential of the first-order neurons of the VIII cranial nerve.

The data obtained from animals in Control Group I indicate that the magnitude of the cochlear response produced by the 1000 cycle tone at the reference intensity did not fluctuate appreciably (± 2 db). The stability of the cochlear response demonstrated by these animals agrees with the data obtained by other experimenters.[15,26] Further, the cochlear and N_1 responses produced by the acoustic click also demonstrated stability through periods as long as 72 hours. Data obtained on two guinea pigs representative of Control Group I are presented in Figure 1. Both animals were anesthetized and body temperature was held constant at the normal level (37° C ± 1°). No chlorpromazine was administered to these animals.

The results obtained on experimental animals injected with chlorpromazine differed from control data, depending upon the presence or absence of body temperature regulation. In Experimental Group I, chlorpromazine did not influence the cochlear or N_1 responses. The body temperature of each of these animals was maintained at the normal level. Figure 2 presents the fluctuations of both responses to the click stimulus for each animal through time.

Unlike the data just cited, chlorpromazine was seen to produce rather dramatic losses in both the cochlear and nerve responses in each of the animals in Experimental Group II. In this group body temperature was allowed to drop until a severe state of hypothermia existed. Thereafter, body temperature was restored to normal. Whether or
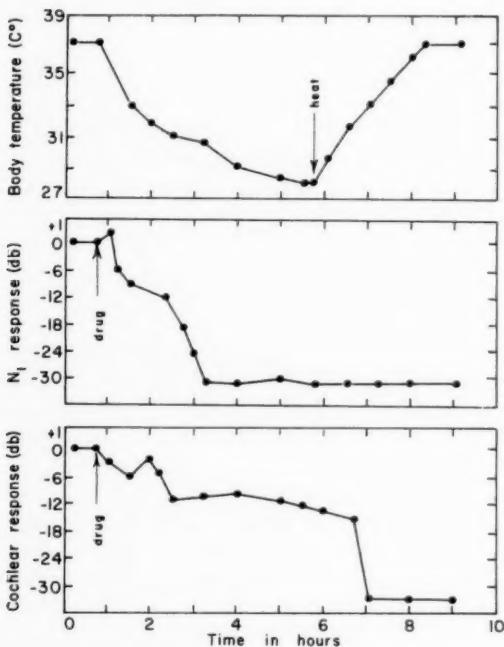
Fig. 4.—Cochlear and N₁ responses obtained to an acoustic click on a guinea pig in Experimental Group II. Responses are given in decibels relative to response magnitudes prior to chlorpromazine administration. The intensity of the click was constant. Body temperature was not held constant and is reported in degrees, C.

not recovery occurred seemed to depend upon the duration and severity of hypothermia. The data obtained on each of two preparations representative of Experimental Group II are presented individually in Figures 3 and 4. The usual pattern of change in the cochlear and N_1 responses produced by the click was a slight facilitation (1 or 2 db) approximately thirty minutes after drug injection, followed by a rapid drop unless it was arrested by the prevention of hypothermia.

The results of drug administration on the preparation shown in Figure 3 include a slight facilitation of the cochlear and N_1 responses after one-half hour. This was followed within two and one-half hours by a drop of approximately 4 db in both responses. Heat was

applied at this time in an attempt to bring about recovery, and within two and one-half hours after heat application both responses had returned to pre-drug levels. A second dose, with body temperature maintained at 36° C failed to effect a change in the responses up until termination of the experiment, three hours after the second drug injection.

Within one hour after drug injection, the cochlear and N_1 responses of another animal in Experimental Group II (Figure 4) had dropped 6 db. Heat was applied four and one-half hours after drug administration in an effort to bring about recovery of the responses. Although body temperature returned to normal within two hours, the responses continued to drop and were completely abolished. No recovery of the responses was evident eight hours after drug administration. Operative procedure was then performed on the other ear, but neither response could be evoked.

Although the amplitude of the N_1 response was affected by the drug in each preparation in Experimental Group II, the latency with which the response followed the cochlear response did not vary from that measured under control conditions. Figure 5 compares the cochlear and N_1 responses in a representative animal under pre- and post-drug conditions. Here it may be noted that the cochlear and N_1 responses were reduced in magnitude under the drug condition as compared with pre-drug control data but the latency (peak to peak) remained constant.

The effect of the drug on the conscious animal was also investigated. The unanesthetized animals in Control Group II were injected intraperitoneally with chlorpromazine 5-10 mg/kg. The results indicate that some reduction in body temperature occurs in conscious guinea pigs with doses of this size. A drop of about 3° C occurred after one hour. Thereafter, the temperature returned to normal.

COMMENT

According to present-day theory, the cochlear response results from mechanical deformation of polarized hair cells of the organ of Corti. It is assumed that the cell contents differ chemically from the endolymph bounding the cell and that the cell membrane provides a selective barrier to ions within and without the cell. Deformation of the hair cell changes the permeability of the cell membrane and allows an ionic flow.
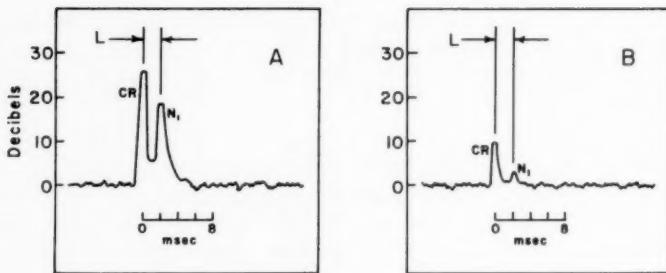
Fig. 5.—Cochlear and N₁ responses recorded from the round window of a guinea pig. The stimulus was an acoustic click. Record A shows the responses before the administration of chlorpromazine, and Record B shows the responses two hours after chlorpromazine was administered (5 mg/kg). The first prominent wave is the cochlear response; the smaller wave is the compound nerve potential, N₁.

In order for sound to be heard, the acoustic nerve fibers must be stimulated. It has been hypothesized that the nerve impulse is set off by the cochlear response.[5,33,34] The acoustic nerve is composed of about thirty thousand individual fibers, and the action potential which arises upon simulation of the nerve is called the compound action potential. The compound potential, as recorded from the round window, is that of the first-order neurons of the VIII cranial nerve. These first-order neurons lead from the cochlea to the first synapse in the cochlear nucleus of the medulla. Since N_1 is the earliest neural event known to occur in the auditory system, it has generally been agreed that N_1 is the sign of the discharge of the first-order fibers of the auditory nerve.[2] A change in its magnitude is ordinarily taken to mean that a corresponding change has occurred in the amount of excitation produced by the sound stimulation.

Possible Explanation of Losses Obtained. Data gathered in the present experiment indicate that when body temperature is maintained at a normal level (37° C) by laboratory control, cochlear and N_1 responses are unaffected by chlorpromazine (5.0 mg/kg). However, when the drug action is permitted to take its course, and body temperature consequently drops, losses in the cochlear response as severe as 32 db were noted. When the cochlear response is reduced, the data show a corresponding reduction in the N_1 responses. Probably the cortical response is also affected, but this remains to be demonstrated.

Full recovery of both responses occurred in most instances in the present study. When recovery was not obtained, it may be that the hair cells in the cochlea were destroyed or irreversibly damaged because of severe hypothermia. Recovery appears to be related to the duration rather than to the degree of hypothermia.

That hypothermia decreases the magnitude of the cochlear response has been demonstrated by Gulick and Cutt.[15] It has also been shown that the amplitude of the nerve response is affected by temperature change. In multifibered frog nerves the amplitude decreased gradually and significantly as the temperature was lowered from 15 to 5° C.[9] In another study in which nerve fibers of cats were cooled, it was observed that as temperature was decreased from 25° to 15° C, the spike amplitude decreased markedly. Subsequent heat application resulted in slight irregular effects.[28]

The reduced circulating blood volume under prolonged hypothermia also may be important. This could produce hypoxemia, a condition known to damage the hair cells in the cochlea.[11] Evidence that changes in oxygen consumption occur with changes in body temperature has been found in cold-room studies.[1] When chlorpromazine treated rats and dogs were placed in room temperatures between 0 and 17° C, oxygen consumption decreased as body temperatures fell, reaching control levels or below at the time of maximum temperature decreases. Accordingly, hypoxia may be a contributing factor to the losses in the present study, but it is doubtful that this alone is sufficient to account for the obtained results since reduced body temperature also reduces oxygen consumption. Furthermore, Gulick[14] concluded that the cochlear response is maintained without serious loss through a wide range of arterial oxygen saturation, and that only when hypoxemia is severe do dire consequences result.

It is clear, then, that sub-normal body temperatures bring about conditions which reduce both cochlear and nerve responses. Moreover, chlorpromazine is known to depress body temperatures in anesthetized animals. Accordingly, temperature variations in this experiment are probably responsible for most of the losses observed under experimental treatment. However, that reduced body temperature is not entirely responsible for the losses observed is evidenced by the results obtained by Gulick and Cutt.[15] Although prolonged hypothermia decreased the magnitude of the cochlear response to a 1000 cycle tone, the diminution of the response in their study was never greater than 11 db, even when body temperature was reduced from 37° C to 24° C. A comparison of their results with those obtained in the present study
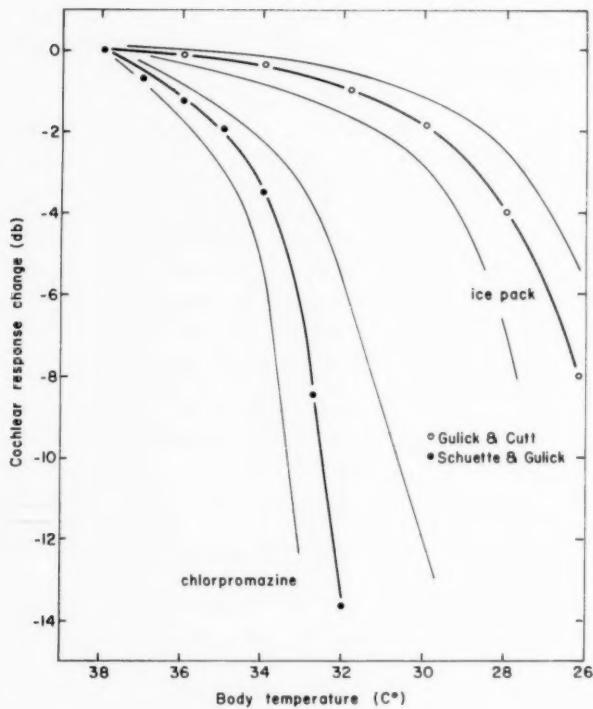
Fig. 6.—Cochlear response to a 1000 cycle tone as a function of body temperature. Each function is based upon data obtained on four guinea pigs. Response magnitudes are given in decibels relative to the response magnitude at normal body temperature. Hypothermia produced by ice pack (after Gulick and Cutt, 1960). Variation is indicated by the boundary lines.

(Fig. 6) indicates that the drug in conjunction with hypothermia produces more severe losses in the cochlear response than hypothermia alone. It may be concluded, therefore, that some additional factor (or factors) beside those operating during hypothermia is involved in producing losses of the magnitude noted in the present experiment.

Possible Sources of Dampening. With body temperature normal, it has been demonstrated that the anesthetic and chlorpromazine do not produce cochlear or N_1 responses which differ in magnitude from those obtained under anesthesia alone. *What remains unexplained is*

the apparent exaggerated losses produced by anesthesia, chlorproma-
zine, and hypothermia as compared with only anesthesia and hypo-
thermia. Based upon data obtained in this experiment, it appears as
though auditory dampening occurring under treatment with chlor-
promazine cannot be attributed to the effects of the drug upon the
peripheral receptor or its first-order neurons. In conscious animals
(Control Group II) maintained in a room at 22° C and injected with
5-10 mg/kg chlorpromazine, body temperature was reduced by only
3° C. The data obtained by Gulick and Cutt[15] clearly indicate that
a decrease in body temperature of this magnitude is insufficient to
affect the cochlear response. It would appear necessary to look else-
where for the source of dampening reported in the literature.

It may be that this drug is affecting some of the higher brain
centers. Killam and Killam[21] suggest that chlorpromazine increases
the effectiveness of the controlling function of the reticular formation.
Moreover, a recent study[20,60] indicates that the reticular formation
exerts some control over the intensity of auditory input by way of
the middle ear muscles. These experimenters noted that reticular
stimulation reduced the amplitude of the cochlear response. However,
after disinsertion of the tympanic muscles from the middle ear ossicles,
reticular stimulation failed to diminish the cochlear response. It is
possible that contraction of the tympanic muscles due to the drug
action on the reticular formation, interacting with hypothermia, could
produce losses of the magnitude noted in this study.

Another source of the dampening may be considered. The drug
may produce its effect by action on the posterior hypothalamus
through the efferent fibers to the cochlea. Chlorpromazine is an
autonomic suppressant which is believed to act by augmenting the
excitability of the posterior sympathetic hypothalamus. When rats
were given 50 mg/kg of chlorpromazine per day, the highest level
of radioactive material was found in the hypothalamus. The concen-
tration of chlorpromazine leveled off or decreased in other brain areas,
but continued to accumulate in the hypothalamus for the duration
of the study.[32] Further evidence of the effect of the drug on the
hypothalamus is found in experiments on self-stimulation of the brain.
Chlorpromazine (2-5 mg/kg) injected about 10 minutes before the
testing period, produced a different pattern of inhibition in the hypo-
thalamus. When electrodes were in the ventral parts of the posterior
hypothalamus, there was heavy inhibition of self-stimulation.[25]

Further evidence of possible sympathetic involvement is the
relative stability of the cochlear and N_1 response when body tempera-

ture is prevented from dropping. Cannon[3] found that complete gangli-onic chains and special sympathetic ganglia could be removed from animals without producing changes in their emotional responses, as long as they were kept in a well-regulated laboratory environment and body temperature was controlled. However, when the animal was exposed to marked changes in temperature, or loss of blood, the deficiencies became apparent.

It would appear advisable, then, to study the effects of chlorpro-mazine on the auditory receptor under several additional experimental conditions. A next step might be to observe drug effects after disinser-tion of the middle ear muscles. Persistence of the suppression would eliminate muscle contraction as a factor. A second step would be to sever the VIII cranial nerve and study the effects of drug administra-tion. A reduction in cochlear response output under this condition would indicate that the drug is producing its effect by some means other than the efferent fibers of the auditory nerve.

SUMMARY AND CONCLUSIONS

The effects of chlorpromazine (5 mg/kg) upon the electrical response of the cochlea and the compound potential of the VIII cranial nerve were observed by recording from the round window membrane of each of five adult guinea pigs. These data were compared with control data obtained from anesthetized and conscious guinea pigs.

On the basis of this study the following conclusions are offered.

1. Chlorpromazine depresses body temperature in conscious gui-nea pigs ($3°$ C) and in anesthetized guinea pigs ($10°$ C).

2. In anesthetized animals chlorpromazine did not produce signif-icant losses in cochlear or N_1 responses as long as the preparation was maintained at normal body temperature.

3. When chlorpromazine was allowed to induce a state of hypo-thermia, marked losses in cochlear and N_1 responses occurred (up to 32 db).

4. Whether or not recovery occurred seemed to depend upon the duration and severity of hypothermia.

5. Under conditions of equal sub-normal body temperature, the losses noted in the cochlear and N_1 responses were more severe when

hypothermia was produced by chlorpromazine than they were when hypothermia was produced by a cold pack.

The data were discussed in relation to possible central inhibitory mechanisms, and the direction of further research was indicated.

UNIVERSITY OF DELAWARE

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XII

EXTRANASOPHARYNGEAL JUVENILE ANGIOFIBROMA

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Juvenile nasopharyngeal angiofibroma has interested and challenged the ingenuity of surgeons since antiquity. The problem of alleviating the suffering caused by this disease has stimulated much clinical and basic research, but today the problem still confronts us. An encounter with this tumor in an unusual location outside the nasopharynx has stimulated this brief clinical report.

A review of 186 cases[1-10] of juvenile nasopharyngeal angiofibroma in the English literature did not reveal any similar case presenting in the cheek without first having widespread nasopharyngeal involvement and its accompanying symptoms.

The classical form of juvenile nasopharyngeal angiofibroma usually presents with symptoms of 1) progressive nasal obstruction, 2) repeated and prolonged epistaxis, 3) purulent rhinorrhea, 4) progressive deformity of the nasal septum, sinuses, palate and face, 5) rhinolalia clausa, 6) anosmia. The tumor is believed by most to be exclusively one of young males,[1] and its onset may be in the middle teens,[2,3] although symptoms may not become serious until the early part of the third decade.

In the case described the only symptoms present were 1) purulent rhinorrhea, secondary to right maxillary sinusitis, 2) progressive enlargement of the right cheek, and 3) occasional dull pain within the right maxilla.

REPORT OF A CASE

This 21 year old white male army private was transferred to Fitzsimons General Hospital on October 6, 1959, with the chief com-

plaint of progressive swelling of the right cheek which was first noted in March 1959. Facial asymmetry had been noted since 1955, but progressive enlargement did not begin until March 1959. The patient occasionally had moderate pain and tenderness of the right cheek, but careful review of systems revealed no progressive nasal obstruction, epistaxis, tinnitus, fullness of the ear, otalgia, difficulty with sense of smell or other symptoms of ear, nose and throat disease.

The past medical history and review of systems revealed previous repair of right cleft lip and palate deformities. At the time of admission the patient had a well-fitting oral prosthesis, and his speech and deglutition were normal. The remainder of the past medical history was noncontributory.

The physical examination at the time of admission to Fitzsimons General Hospital was within normal limits except for the well healed and well repaired deformities of the lip and palate. There was a firm mass present within the right cheek and palpation through the mouth revealed that the mass extended posteriorly toward the right pterygo-maxillary space. The skin over the mass was freely movable. The parotid gland was not involved and functioned normally. There was marked deviation of the nasal septum to the right. Nasopharyngeal examination with the nasopharyngoscope revealed no evidence of tumor mass in the nasopharynx. Careful examination of the neck revealed no significant adenopathy.

The laboratory examinations, including CBC, urinalysis, cardiolipin microflocculation, and chest x-ray were within normal limits. Paranasal sinus x-rays (Fig. 1) revealed opacification of the right maxillary sinus and medial displacement of the lateral wall of the right antrum. There appeared to be no bony erosion of the lateral wall of the right antrum; a soft tissue mass seemed to fill the right cheek area and extend posteriorly toward the right pterygomaxillary space. No mass was visible in the nasopharynx on lateral views of the skull. A right parotid sialogram was within normal limits and showed no involvement of the right parotid gland by the tumor mass.

A pre-operative diagnosis was made of soft tissue tumor of the right cheek with extension or origin in the right pterygomaxillary space. The patient was taken to surgery on October 12, 1959, where under general endotracheal anesthesia an incision was made in the right buccogingival fold. At the time of surgery a large vascular tumor was shelled out of the right cheek (Fig. 2), the infratemporal fossa, the right temporal fossa and the right pterygomaxillary space. The tumor mass extended into the right parapharyngeal space where
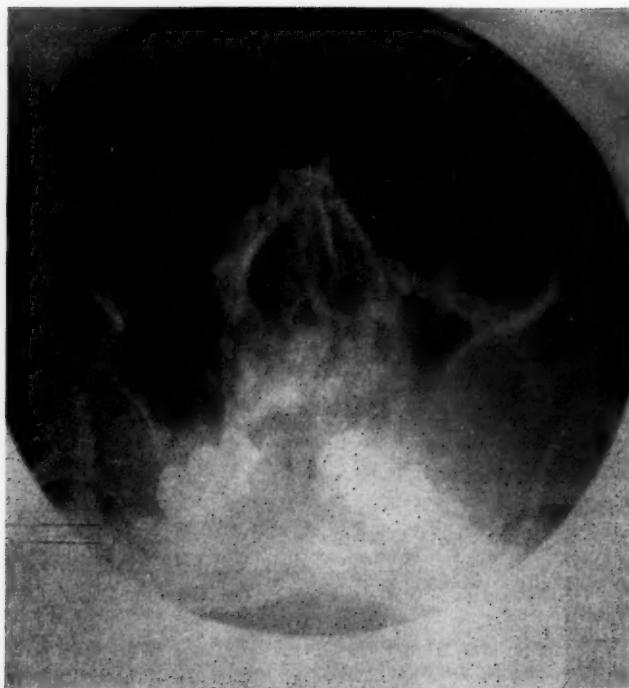
Fig. 1.—Pre-operative x-ray showing medial displacement of lateral wall
right maxillary sinus and soft tissue mass within right cheek.

it appeared to be attached to the medial pterygoid plate.   Upon
exposure of the tumor a tentative operative diagnosis of juvenile
angiofibroma was made, and this was subsequently confirmed by
frozen pathological section.   The tumor shelled out rather easily and
only moderate hemorrhage was encountered.   Nasopharyngeal exam-
ination at the time of surgery with the palate retracted, using nasal
catheters and a laryngeal mirror, revealed no abnormalities of the
nasopharynx except for the mucosal rent anterior and inferior to the
right eustachian cushion.   A right antral window was attempted and
tissue was cut away from beneath the inferior turbinate.   However,
subsequent pathological examinations revealed this to be juvenile
angiofibroma rather than medial antral wall.   Postoperatively, the
patient did well; an estimated blood loss of 1000 cc was replaced with
an equal amount of whole blood.   The gross tumor (Fig. 3) measured

Fig. 2.—Operative photograph after exposure of tumor mass within right cheek.

Fig. 3.—Gross operative specimen.
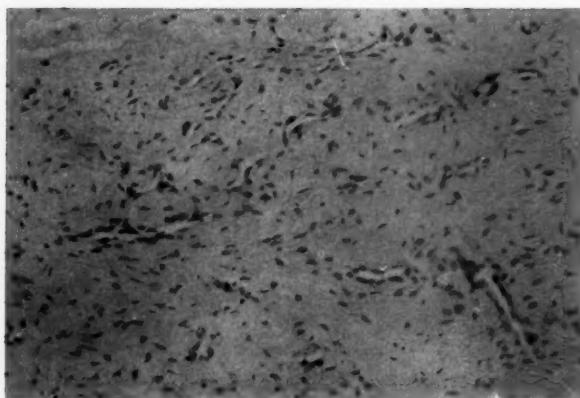
Fig. 4.—Photomicrograph of the pathological specimen.

9 x 4 cm and microscopic examination (Fig. 4) confirmed the frozen section diagnosis of juvenile angiofibroma. The patient was tube fed for eight days, and on the eighth postoperative day the nasal packing and feeding tube were removed. Examination of the nasopharynx was within normal limits at this time except for polypoid degeneration of the posterior tip of the right inferior turbinate. Examination of the nose revealed a small tumor mass beneath the middle turbinate. Pathological examination of the biopsy specimen of this tissue showed juvenile angiofibroma. Pathologic diagnoses were confirmed by the Armed Forces Institute of Pathology. Postoperatively, the patient continued to do well and re-examinations of the nasopharynx revealed no further abnormalities. The patient was given convalescent leave until December 1, 1959, and at this time he reported that he was asymptomatic. Complete ear, nose and throat examination revealed no abnormalities except for the previously mentioned polypoid degeneration of the posterior tip of the right inferior turbinate. At the time of discharge from Fitzsimons General Hospital the patient was entirely asymptomatic.

COMMENT

The origin of juvenile nasopharyngeal angiofibroma is debated, with the majority of earlier reports favoring the tissue of origin as the embryologic chondro-cartilage at the base of the skull.[5,11] More recent

reports dispute this theory. Brunner in 1942[6] contended that the juvenile nasopharyngeal angiofibroma arises from the fascia basalis (merger of the pharyngeal aponeurosis and buccopharyngeal fascia) and not from the periosteum of the base of the skull. In 1954 Sternberg[7] analyzed a series of 25 cases from Cancer Memorial Hospital and stated, "This tumor represents a distinctive variety of angioma with a unique stroma and stromal cell—these tumors are sex and age linked and probably influenced by some as yet unknown endocrine factors." Hubbard in 1958[1] basically agreed with this last opinion.

Schiff postulates,[5] "This tumor is due to an alteration in the androgen-estrogen axis most probably involving overactivity of the pituitary and reflecting itself in a ground substance response to a vascular tumor." He further states that the exclusive location within the nasopharynx is due to hormone sensitive tissue of the inferior turbinate being located ectopically within the periosteum of the base of the skull and a desmoplastic response occurs at the time sensitizing hormones begin to circulate (puberty). Further studies are necessary to determine which of the many theories are correct. We feel the last theory (Schiff) opens the door for possible improved therapy of this dangerous entity, but as yet no theory has completely explained the peculiar behavior of this neoplasm.

It is interesting to speculate as to why the case reported did not present within the nasopharynx, and what part did the congenital cleft palate and lip with its accompanying maxillary deformity play in the unusual form of presentation of this tumor? Certainly one can suspect that ectopic tissue may have become located farther afield than normally, and this may have been the cause of the extranasopharyngeal location. We have not been able to determine from the cases reviewed if any other case of nasopharyngeal angiofibroma has occurred in a patient with a cleft palate deformity. Consequently one can only speculate as to the relationship, if any.

The treatment of juvenile nasopharyngeal angiofibroma has taken many forms which include 1) x-ray, 2) radium implantation, 3) local sclerosing solutions, 4) endocrine therapy, 5) electrocoagulation, 6) surgical treatment, and 7) combinations of above. The problems of therapy are many and each method has its advocates. We feel that today endocrine therapy and surgery offer the best chance for cure.

The view of spontaneous regression of these tumors during the third decade was held for many years[2] but more recent articles[1,3,7,9] do not substantiate this optimistic viewpoint. We concur with Schiff[5]

"that waiting for the expected involution of this tumor is but to wait for the tumor to grow bigger and present more problems at a later date." Each case must be considered individually and therapy planned accordingly. Today with earlier patient-physician contact, improved surgical technique and anesthesia, we should see an improving cure rate.

SUMMARY

An unusual case of extranasopharyngeal juvenile angiofibroma is presented with a brief discussion of theories of origin and treatment of these interesting tumors.

FITZSIMONS GENERAL HOSPITAL

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XIII

DELAYED COCHLEAR DAMAGE
IN STAPES SURGERY

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The purpose of this paper is to evaluate the delayed cochlear damage in the surgical treatment of otosclerosis. This is usually seen a few weeks after surgery. In some cases, it could be delayed as late as nine months.[3] In early papers it has been described as due to serous labyrinthitis; Farrior[2] wrote that it could be due to mucous or chemical labyrinthitis. In a recent article, Schuknecht[6] described delayed cochlear degeneration as of unknown etiology.

Among 120 stapes mobilizations done in our clinic last year by different methods, three cases developed delayed cochlear damage.

REPORT OF CASES

CASE 1. Mr. G.B., aged 55, was seen for marked tinnitus and marked hearing loss, had been hard of hearing for fifteen years.

Clinical examination revealed essentially normal findings and the audiogram a pronounced conductive hearing loss (Fig 1). Stapes mobilization was performed on January 12, 1960. Tympanotomy revealed fixation of the anterior crus of the stapes and the anterior portion of the footplate. Stapedectomy and mobilization of the footplate were done and a polyethylene strut was placed over the footplate and fitted to the incus. Postoperative recovery was uneventful. On January 21, 1960, the audiogram revealed a moderate improvement for speech frequencies. Three weeks after surgery the patient developed a positional vertigo and hearing loss. On May 17, 1960, a diagnostic tympanotomy showed a slight depression of the footplate posteriorly and a small fistula at the center of the footplate where the strut had been placed. A very small amount of perilymph was seen escaping through the fistula. In view of the decreased bone conduction, the mucosa over the horizontal portion of the Fallopian canal and the promontory was denuded and a vein graft taken from the hand was used to cover the fistula and the denuded area. A
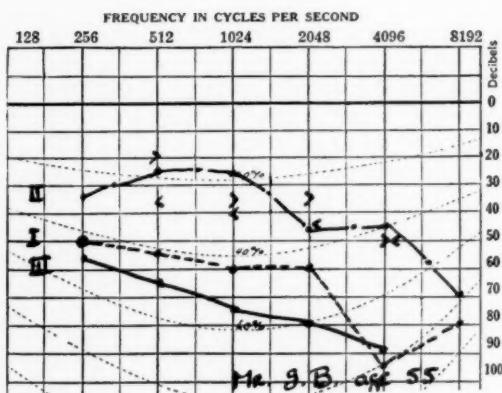
Figure 1

>   Preoperative bone conduction
<   Bone conduction four weeks after surgery
I   Air conduction before surgery
II   Air conduction one week after surgery
III   Air conduction four weeks after surgery

shorter polyethylene tube was placed over the graft and fitted to the lenticular process of the incus. The postoperative condition was good, with no further vertigo. Repeated audiograms revealed no drop in hearing during the last three months.

CASE 2. Mrs. E.F., aged 56. This patient was seen regarding progressive hearing loss and marked tinnitus which she had had for 25 years. Ear, nose and throat examination was essentially normal. The audiogram (Fig. 2) revealed a marked conductive hearing loss. On March 16, 1960, inspection revealed fixation of the anterior crus of the stapes and the footplate by otosclerotic bone. Stapedectomy with mobilization of the footplate was done and a polyethylene strut was used. The postoperative period was without any complication. On April 4, 1960, an audiogram revealed narrowing of the air-bone gap. On April 25, 1960, she developed positional vertigo and hearing loss. A diagnostic tympanotomy was done; during infiltration of the external auditory canal with local anesthetic (Xylocaine 2%), she developed violent vertigo and nausea. The tympanotomy revealed a central fistula of the footplate, larger than in the first case. Leakage of the perilymph into the middle ear was observed. The fistula was closed with the vein graft as described in the first case. The postoper-
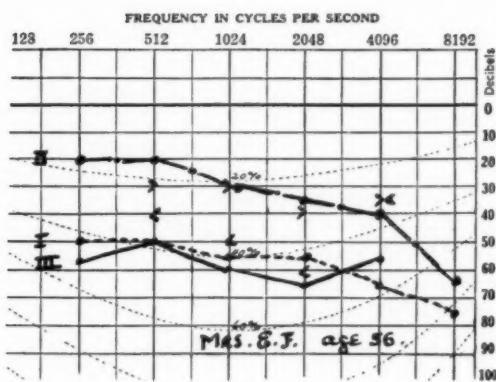
Figure 2

>   Preoperative bone conduction
<   Bone conduction April 25, 1960
I   Preoperative air conduction
II   Postoperative air conduction
III   Air conduction April 25, 1960
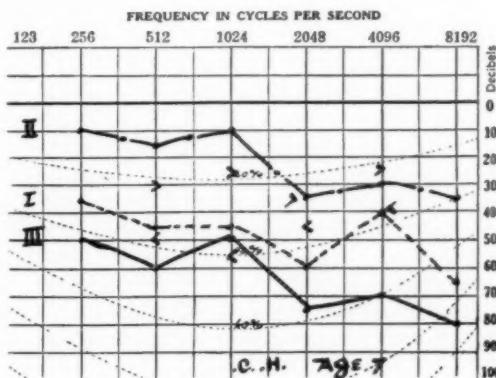
Figure 3

>   Preoperative bone conduction
<   Bone conduction July 28, 1960
I   Preoperative air conduction
II   Postoperative air conduction
III   Air conduction July 28, 1960

ative condition was without complication.   No vertigo or hearing loss
has been observed since the second operation.

CASE 3.   C.H., aged 6.   This patient was seen on August 15,
1959.   The child's parents complained that he did not hear too well.
Findings were normal except that the left tympanic membrane did
not move well with insufflation.   The nasal smear revealed 75%
eosinophiles and the audiogram (Fig. 3) showed mixed deafness.
Diagnostic tympanotomy on August 27, 1959, showed fixation of the
stapes by fine fibrous tissue; a very small cyst-like structure and
hyalin-like deposits were observed on the footplate.   The footplate
seemed to be decalcified.   The stapes was mobilized, and the postoper-
ative course was uneventful.   The audiogram on September 2, 1959,
revealed air-bone gap-closure.   This case was diagnosed as adhesive
otitis.   The patient was seen again on July 28, 1960.   The child's
mother noticed that it was not hearing as well during the past month.
Ear, nose and throat findings were negative except that the tympanic
membrane did not move adequately.   The audiogram showed a marked
drop in hearing.   Further history revealed no dizziness or nausea after
the operation.   Roentgen examination of the internal auditory mea-
tuses was negative, but there was speech discrimination showing severe
loss.   Diagnostic tympanotomy revealed complete disappearance of
the previous disorders.   The footplate seemed to be normal, no discol-
oration was observed.   The posterior crus of the stapes was found
fixed and posterior crurotomy was done.   The child was discharged
on the following day.

COMMENT

In Cases 1 and 2 the fistula formation was responsible for the
delayed cochlear damage.   The complete disappearance of the symp-
tom following the second operation confirms this.   The fistula forma-
tion was due to pressure necrosis as the result of using a strut that was
too long.   In these cases as a result of the fistula amplified vibratory
energy or leakage of perilymph is responsible for the delayed cochlear
damage.   The delay is measured by the time required for the develop-
ment of the fistula.   Certainly it is obscure when the symptoms occur,
either during the transmission of increased vibratory energy or during
the leakage of perilymph.   Both may be responsible simultaneously.
Experimental studies on cats[7] show cochlear damage by fracture of
the footplate in fistula formation as late as 290 days without profound
damage to the cochlea.   Experimental studies[4] reveal cochlear damage
by rupture of Reissner's membrane as a result of amplified vibratory
energy.   I believe these experimental studies favor the increased vibra-

tory energy, as a result of the fistula, as causing the destructive changes in the cochlea.

The third case is interesting for the disappearance of the middle ear pathology considering the allergic status of the patient, the role of allergy may be responsible for production of the middle ear disorders and probably for the cochlear damage. Bellucci and Wolff[1] observed degenerative changes in the cochlea after placing gelfoam over the oval window. They suggested that chemical toxic factors caused the degenerative changes in the cochlea.

Considering the marked delay and the absence of vestibular symptoms, toxic etiology may be responsible for the cochlear damage in the third case.

In cases of delayed cochlear damage the importance of diagnostic tympanotomy is obvious. Fistula formation or a too long strut, or prolapse of the graft or the vein graft, may be responsible for delayed cochlear damage. In cases in which cochlear damage is long delayed, toxic factors or other biochemical factors may be responsible.

When fistula formation is suspected, topical anesthetics[5] should be carefully selected.

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ELECTRONYSTAGMOGRAPHIC STUDIES
OF VESTIBULAR FUNCTION:

IV. INVESTIGATION OF THE BEHAVIOR AND SIGNIFICANCE OF VARIOUS NYSTAGMUS QUALITIES FOR THE DETERMINATION OF NORMAL VESTIBULAR REACTION

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In previous papers[1,2,16,17] an attempt was made to establish reliable procedures of electronystagmographic (ENG) recordings for quantitative evaluation of certain basic qualities of the complex nystagmic eye movements.[2] The ENG recordings were obtained with the EEG apparatus Grass Model III D by picking up corneo-retinal potential changes with contact electrodes suitably placed around the eye.[16]

Subsequent investigations attempted to evaluate the significance of the various basic qualities of nystagmus in response to specific vestibular stimulation. Using the same apparatus and method of recording, normal and abnormal vestibular functions were investigated. Results obtained on 40 normal ears with bitemporal electrodes[16] will be discussed in this paper.

Caloric vestibular nystagmus was recorded with the EEG apparatus, using a stimulus of 10 cc water at 70° F which was injected into the external auditory canal within 10 sec. The subject's head was flexed backwards and kept in optimal position (60° from the horizontal plane) for the entire duration of the vestibular reaction. External and internal artifacts were reduced by dark adaptation, complete relaxation, Frenzel goggles, etc., as described in our previous papers.[2,16] The duration of nystagmus was recorded from the onset of stimulation. Therefore, it includes the stimulation period of 10 sec.

Normal ears used for this investigation were selected according to the following requirements: 1) normal physical and mental health; 2) undisturbed and relaxed state of mind; 3) normal hearing function in the tested ear; 4) normal results of routine vestibular tests for both ears when some sensori-neural hearing loss was present in the opposite ear; 5) no external and middle ear pathology which may change heat conduction towards the labyrinth; 6) no optokinetic abnormalities (ocular nystagmus, paralysis of eye muscles, previous operations on eye muscles, etc.).

The individual results obtained from these 40 normal ears were averaged and treated by simple statistical methods. For controlling the results, a further statistical treatment was performed with the results of 12 subjects with bilaterally normal ears.

Depending upon the total duration of the nystagmic response, a sufficient number of sample periods are selected from the ENG tracing, obtained for the entire nystagmic reaction with methods as specified above (Fig. 1). Each sample period contains a group of successive nystagmus beats for time segments of three to ten seconds. Periods of five seconds are preferred. The samples are selected from suitable parts of the ENG tracing which are free from disturbing additional eye-movements (blinking,[16] convergent eye movements,[16] eye undulations, etc.). Furthermore, these samples should be evenly distributed over the entire nystagmus duration in order to be representative of the true pattern of the complete nystagmic reaction. With this method, about 1/4 to 1/5 part of the entire tracing is evaluated. Additional samples are taken if the original selection was insufficient for giving a clear picture of the nystagmic pattern.

For each sample period the 1) average frequency, 2) average amplitude, and 3) their product are then determined according to the principles described previously.[2,16,17] Using very short time constants (0.05 sec), a record of the velocity of the fast nystagmus component is obtained. After proper calibration of the amplifying system, the nystagmus amplitude is computed from this velocity tracing. The amplitude thus obtained is that of the fast nystagmus component. Since the average amplitudes of the fast and slow nystagmus components can be considered equal for a given sample period, the obtained amplitude of the fast component is equal to the amplitude of the slow component.

The product of the average amplitude and frequency is a particular type of angular velocity of the nystagmic eye movement for which
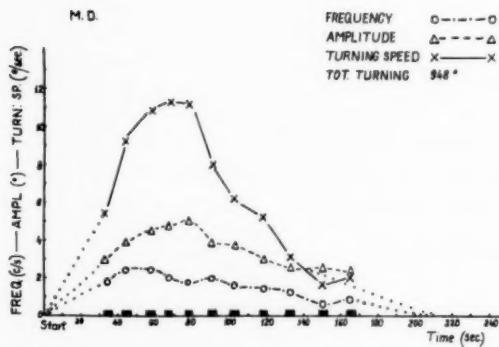
Fig. 1.—*Normal turning-speed curve* (x——x) with the respective frequency (o——•——•——o) and amplitude ($\triangle$ - - - $\triangle$) curves. On the abscissa, the duration of the nystagmus is plotted from the start of stimulation. The graduation of the ordinate expresses the values of frequency in cycles per second, of amplitude in degree, and of turning speed in °/sec. ■ indicates the sample period. Total turning, 948 degrees. Dotted lines: extrapolation of the curves. (Reprinted from *Trans. Am. Acad. Ophthalm. and Otolaryng.*)

the term, "turning-speed," is suggested. It indicates the theoretical rotation of the eye within the time unit, by adding all single nystagmus beats for one second, as if the slow phase of nystagmus were a continuous movement and the saccadic backrolling of the eye (fast phase) were excluded from the nystagmus. Since the turning speed is computed by multiplying average amplitude and average frequency, its value represents the average value of the respective sample period.

The use of a special denominator for the description of the computed angular velocity is indicated by the fact that the value of turning speed is slightly smaller than the actual speed of the slow nystagmus component for the same nystagmus. Results of velocity computations that are derived from the average amplitude and frequency of a given sample period contain time segments which exceed the duration of the slow component and include time elements which belong to the fast component (Fig. 2).[9-11]

The amplitude of nystagmic eye movements can be determined either from the *amplitude,* or from the *territory of the spikes* which represent the nystagmus beat in the ENG tracing.[2] Consequently, the value of turning speed as the product of amplitude and frequency can be obtained by determining either the amplitude or the territory
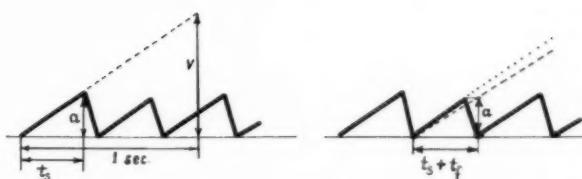
Fig. 2.—Difference between the *turning-speed* value and the *angular velocity* of the slow nystagmus component. The decline of the nystagmus tracing indicates the velocity: in the left figure, - - - - is the velocity of the slow component; in the right figure, - - - - is the turning speed compared to the velocity of the slow component (. . . .). a = amplitude; t_s = duration of the slow component; $t_s + t_f$ = duration of the entire nystagmus beat. (Reprinted from *Trans. Am. Acad. Ophthalm. and Otolaryng.*)

of the recorded spikes. For the reduction of computational errors, a double determination of the turning speed values was performed by deriving them from both the amplitude and the territory of the spikes.

The results of average frequency, average amplitude, and average turning speed for each respective sample period are then plotted in a graph as a function of the duration of vestibular reaction. The respective curves for each of these quantities are then composed by connecting the individual results. In that way, separate curves for the frequency, amplitude, and turning speed pattern are obtained for the described vestibular reaction (Fig. 1).

TOTAL DURATION OF NYSTAGMUS

None of the three curves begins or ends at the time axis (baseline). The recorded onset and end of the nystagmic response are subject to the sensitivity and liminal level of the particular method of registration or observation used. This liminal level represents the weakest discernible nystagmus beat which can be distinguished from any artifacts in the tracing.[16] In other words, it indicates the smallest eye movement that can still be differentiated in the ENG tracing from other bio-electric features which are also picked up by the electrodes and appear as smaller or wider oscillations of the baseline.

For these reasons, the total duration of the reaction seems to last longer than indicated by the actually observed final nystagmus beat.

Therefore, an extrapolation of the frequency and turning speed curves, as plotted in our figures (Fig. 1), has been considered a better approach for the determination of the end of reaction than the observation of the last discernible nystagmus beat. Such extrapolations can be considered especially correct if these two curves reach the time-axis around the same point. In some cases, also the third curve, the amplitude pattern intersects the time-axis at a nearby point; however, the decline of the amplitude curve does not follow as regular a pattern as found for the curves of frequency and turning speed (see below).

Observations on the latency of nystagmus revealed similar circumstances as described for the nystagmus decay. If the zero point on the time-axis is connected with the various values obtained for the first sample period, these extrapolations result in an even continuation of all three curves. The shape of our curves led us to believe that the latency also depends on the sensitivity and liminal level of the particular observation, and that its duration is likely to be much shorter than would appear from the onset of the observed first nystagmus beat.

Another obstacle involved in our method in recognizing the first nystagmus beat is due to increased bio-electric activity which occurs right after the stimulation with cold water. This is caused by discomfort, tension, defensive movements, etc. These transitory artifacts render the tracing unsuitable for nystagmus evaluation for at least several seconds after stimulation. Because of all these difficulties, the latency of the nystagmus has not been evaluated in the presented series of cases.

The total duration of a nystagmic reaction to caloric stimulation as defined above, showed an average value of 208.0 ± 6.42 sec, with a standard deviation of ± 39.9 sec, and a median of 197.2 sec. When considering the series of 24 bilaterally normal ears separately, we obtained an average of 214.79 ± 9.52 seconds.

FREQUENCY PATTERN OF NYSTAGMUS

The frequency of the nystagmus beats, computed as the average for each respective sample period, shows a curve with an ascending and a descending slope. The peak of this curve is reached after an average of 64.8 ± 3.42 sec from the onset of stimulation; on its peak, it shows an average value of 2.5 ± 0.1 cps sec. The distribution of these values presents fairly high scattering, especially the position of the peak-frequency on the time axis (stand. dev. ± 21.6 sec). This indicates that the frequency pattern of nystagmus after identical
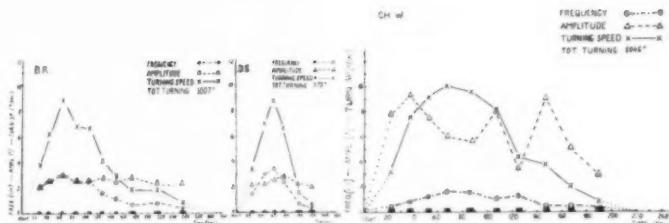
Fig. 3.—*Comparison* between one of the longest and shortest normal vestibular reactions. Symbols are the same as in Figure 1, but the time axis is reduced to ½. Note the shape of amplitude and frequency curves and their relationship.

Fig. 4.—*Normal turning-speed curve.* Symbols are the same as in Figure 1. Total turning: 1046 degrees. Note the interdependent oscillations of the amplitude and frequency curves, the secondary peaks of the amplitude curve, and the relatively high amplitude pattern. (Reprinted from *Trans. Am. Acad. Ophthalm. and Otolaryng.*)

stimulation may show a variable course which depends on individual differences and interrelations to be discussed later.

This variability may cause irregularities of the frequency curve such as a delayed peak, multiple peaks, etc. (Figs. 4, 5). However, the general trend of the frequency pattern appears as just described. At the end of the reaction, the frequency decreases gradually in a curve which declines to the base line (Fig. 1).

The integration of the frequency curve resulted in the total number of nystagmic beats for the entire duration of vestibular reaction. The average frequency was obtained from the ratio of the total number of beats to the total duration of the reaction. The peak values were read directly from the graph.

An apparent rise of the nystagmus frequency at its peak (2.5/sec) in relation to the average frequency for the entire reaction (1.3/sec), is a characteristic feature of the frequency pattern which has already been demonstrated by Torok.[21] This is in contrast to the more even curve of the amplitude pattern (Fig. 3).

AMPLITUDE PATTERN OF NYSTAGMUS

The amplitude of nystagmus, expressed as the average for each sample period, also shows an ascending and a descending tendency. However, the amplitude curve appears flatter (Fig. 3) and much more
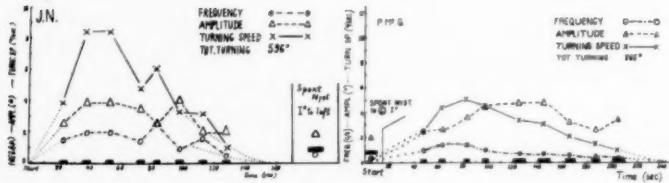
Fig. 5—*Slightly reduced vestibulogram.* J.N., 25, female, with slowly progressive, bilateral, sensorineural hearing loss. Normal duration values with routine caloric and turning tests. Note a secondary peak of the turning-speed curve and the interdependent amplitude and frequency variations. Symbols are the same as in Figure 1. The values of spontaneous nystagmus (I° to the left) are plotted on the right side of the graph: △ = amplitude; o = frequency; ■ = turning-speed.

Fig. 6.—*Vestibulogram in a case of progressive hereditary inner ear lesion* with recruiting sensorineural hypoacusis in both ears. Normal duration values with routine caloric and turning tests. Symbols are the same as in Figure 1. Total turning, 555 degrees. The values of spontaneous nystagmus (I°) are plotted on the left side of the graph: △ = amplitude; o = frequency; ■ = turning speed. Delayed amplitude peak and high amplitude values in the decaying period of vestibular reaction. (Reprinted from *Trans. Am. Acad. Ophthalm. and Otolaryng.*)

irregular than the frequency curve. This is indicated by the increased standard deviation (± 33.4 sec) for the position of the peak on the time axis average: 69.4 ± 5.64 sec. In some cases, the amplitude curve had several peaks (Figs. 4, 5), or the peak value appeared in the end portion of the curve when the nystagmus was already fading away and when all other nystagmus qualities showed gradually declining values (Figs. 5, 6).

There are two different types of amplitude and frequency variations to be distinguished from each other: 1) the independent variations of nystagmus amplitude and frequency appear as the ascending and descending limb of its course (Fig. 1); 2) the amplitude curve indicates a marked interdependence with the frequency changes. For the same subject and during the same reaction, the curves of amplitude and frequency show deviations in opposite directions to each other. The frequency decreases when amplitude rises, and vice versa (Figs. 4, 5). The interrelation of the amplitude and frequency patterns becomes especially apparent when comparing the course of respective individual curves (Fig. 3).

We gained the impression that there are individual differences in the amplitude vs. frequency relationship of nystagmic response. One

subject may show a greater amplitude response *re* frequency pattern, and the opposite may be seen in another case (Figs. 1, 3, 4, 6). The cause of this variable interrelation of amplitude and frequency may be found in the very complex competitive balance between the propelling vestibular reflex during the slow phase and the centrally elicited back-pulling fast phase.

The peak values of amplitude (in average: $4.93 \pm 0.36°$) were read directly from the graph. However, the average amplitude could be obtained only indirectly, since the amplitude curve does not always present a declining slope which tends to reach the baseline by extrapolation (Figs. 3, 5, 6, 7). Therefore, the average amplitude was obtained by the ratio of total turning to the total number of nystagmus beats of the vestibular reaction ($3.33 \pm 0.17°$).

As has been shown, the amplitude and frequency of nystagmus do not seem to be independent qualities. Consequently, either one alone can hardly be regarded as an exact measure of the nystagmic response to vestibular stimulation without considering and recording the changes of the other quality. If we attempt to express the vestibular response in a simple manner as a function of one single quantity, it will be necessary to investigate further nystagmus qualities.

TURNING-SPEED PATTERN OF NYSTAGMUS

In contrast to the above described variable interpendence between amplitude and frequency, their mathematical product, i.e. the turning-speed, shows a considerably more regular curves in the course of the caloric vestibular reaction (Figs. 1, 3, 4, 6). As shown in Figures 4 and 6, the interdependent and accidental variations of amplitude and frequency are equalized in the turning-speed curve. Its slope presents a gradual rise during the first 1/3 of the reaction, then a peak, and lastly a gradual decrease during the final 2/3 of the reaction time. The slope of this curve is much more stable than that for both the frequency and amplitude pattern. Secondary peaks in the turning-speed pattern are seldom observed (Fig. 5). The average peak value of turning-speed was $9.7 \pm 0.8°$/sec, and occurred 61.5 ± 1.66 sec after the start of stimulation. The position of the peak value on the time axis shows less scatter (± 10.5 sec stand. dev.) than the peak values for frequency and amplitude. Rossberg[19] came to the same conclusion in finding that the speed of the slow component shows a considerably more constant pattern during the vestibular response than does its amplitude, which may vary from one jerk to the other within fairly wide limits.
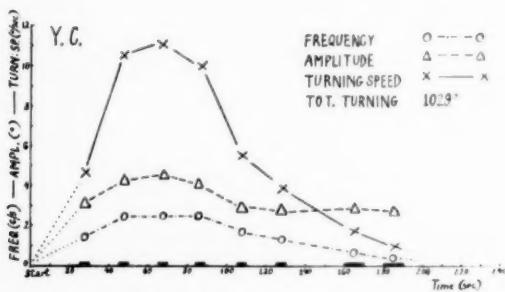
Fig. 7.—*Normal turning-speed curve.* Symbols are the same as in Figure 1. Total turning: 1029 degrees. Note the amplitude curve which forms a plateau in the decaying period of the vestibular reaction.

We gained the impression that the peak part of the turning-speed curve is determined by variations of both the nystagmus frequency and amplitude. Towards the end of the reaction, however, the frequency pattern is of greater influence on the shape of the turning-speed curve. In the final stage of the reaction, the frequency curve fades away gradually (Figs. 1, 3, 4, 6), whereas the amplitude curve sometimes remains on a constant plateau without a gradual decline, as was described before (Figs. 3, 7).

For the past 25 years, scattered information appeared in the literature concerning the speed factors of the vestibular nystagmus. During the early days of nystagmography, Buys[4] and Dohlman[5] observed that the speed of the slow component of vestibular nystagmus is proportional to the intensity of a vestibular stimulus. This stimulus may be applied either as an angular acceleration on a rotating chair, or as a temperature difference between the subject's ear and the irrigating water. Many other authors confirmed this opinion and emphasized the importance of recording the ocular speed for the purpose of testing a vestibular function. Egmond et al.[6] demonstrated a direct proportion between the cupula deflection and the speed of the slow component.

In 1955, Henriksson[9-11] developed a method of ENG by means of a modified EKG system which records the speed of the slow component directly by proper selection of the time constant and by rectifying the corneo-retinal potentials. In this manner, the speed of the slow component of induced nystagmus may be automatically recorded, presenting a characteristic curve as a function of time. These derived

and rectified tracings were similar to the curves published earlier by Boenninghaus,[3] Dohlmann,[5] and others.

Should the cupula deflection really show a linear relation to the speed factor of the effector organ, the basic question of quantitative vestibular investigations could be solved quite easily. Similar to all other sensorial investigations, the basic question involved here is the relation between stimulus and sensation (or any equivalent of the sensation). In eliciting a reactive vestibular nystagmus, two consecutive mechanisms are involved. One is the cupula deflection in primary response to the stimulus, and the other is some appropriate quality of the nystagmus in secondary response to the cupula deflection.

If the nystagmic response shows a linear relationship to the cupula deflection, as is assumed when the nystagmus is measured by its speed factor, the quantitative effect of the stimulus on the primary cupula deflection can easily be evaluated by recording the turning-speed of the nystagmic response. Therefore, the graphic plot of turning-speed as a function of nystagmus duration is called the "vestibulogram." This particular term should also distinguish this specific graph of the speed factor from any other types of nystagmogram as obtained by the various methods described in the literature.

To formulate a mathematical expression of the shape and height of the turning-speed curve, two ratios have been employed: 1) the ratio of the *total turning* value (see below) to the *peak turning speed* value; and 2) the ratio of the *peak turning speed* to the *average turning speed* of the entire vestibular reaction. The normal values of these two ratios (94.8 ± 3.44; 2.3 ± 0.09) will serve for the subsequent evaluation of abnormally shaped turning-speed curves.

The turning-speed curve describes the nystagmic response in two dimensions (Figs. 3-9):

1) The time-factor represents its duration along the horizontal time-axis; this is the distance on the time axis from the onset of vestibular stimulation to the extrapolated end of the curve where it blends into the time axis.

2) The "intensity" factor (intensity of nystagmus) is defined by the vertical axis, i.e. by the value of the turning-speed.

This has a maximal value at the peak of the curve and several authors consider this peak-value as the intensity of nystagmus.[19] We

feel that the "intensity" of nystagmus should be distinguished from the magnitude of a vestibular reaction as observed in its nystagmic response.

Therefore, we consider not only the peak value of turning speed as the "intensity" of nystagmus, but also all other values of the turning speed in the course of a given vestibular reaction. Thus, the "intensity" of nystagmus changes as the vestibular reaction increases and decays. Its peak value may give some indication with respect to the magnitude of the vestibular reaction. However, this magnitude will be expressed by another value which comprises both the intensity and time components of the reaction, as will be discussed below.

By means of the turning-speed determination we can define not only the "intensity" of a time dependent *reactive* nystagmus, but also that of any infinite *spontaneous* nystagmus (Figs. 5, 6). In other words, the turning-speed serves for the comparison and evaluation of both reactive and spontaneous vestibular nystagmus; thus, the magnitude of both can be expressed by means of one single term.

TOTAL TURNING

Both dimensions, the duration and the "intensity" factor of a reactive nystagmus together describe the vestibular response. It has been suggested, therefore, that the magnitude of the vestibular response (to be distinguished from the "intensity" of nystagmus) should quantitatively be defined by the product of both. This product is derived from the integration of the entire turning-speed curve, and is represented by the area bounded by the turning-speed curve and the base line. This is called the "total turning" (total amplitude) of the nystagmic eye movements. The total turning indicates the number of eye revolutions in degrees which would theoretically occur during the entire vestibular reaction, if the slow nystagmus component consisted of a continuous eye rotation without being interrupted by the saccadic backrolling of the eyes in the fast nystagmus phase. We feel that the total turning may very well define the quantity of a vestibular response to a given type of stimulation.

The average total turning for the specific caloric stimulation used was 897 ± 77 (stand. dev. ± 486) degrees for normal ears. This means that the eye would turn 2.5 times around its axis if the fast backrolling could be excluded from the nystactic movements, and if eyes could rotate freely like a suspended globe.

TOTAL NUMBER OF NYSTAGMUS BEATS

The total number of nystagmus beats simply represents the sum of all nystagmus beats in the course of a vestibular reaction. It is derived from integration of the frequency curve.

We wish to emphasize that both the total number of nystagmic beats, and the total turning are derived quantities. They are obtained through computations from the average values of frequency and amplitude for selected sample periods, and not by measurements through direct observation. That is why these values may contain errors not only of measurement but also of derivation.

COMMENT

Among the three time dependent factors (frequency, amplitude, and turning-speed) and the three summarizing factors (total duration, total turning, and total number of nystagmus beats), the turning-speed and its plot (i.e. the vestibulogram) seem to be the most important for practical purposes.

Obviously, the more details are elaborated, the more information is obtained for the description of certain biological functions. However, this elaboration of details is limited by requirements of practical applicability. If the attempts at objective registration of vestibular phenomena are to gain acceptance by the practicing otologic profession, a condensed summarizing description of the vestibular reaction will be required. This should be in the form of a handy graph which clearly demonstrates differences between normal and pathologic findings, and expresses these differences in appropriate quantitative terms.

The turning-speed curve and its graphic plot proved their practical usefulness for routine vestibular evaluation, as will be discussed in a subsequent paper. From the viewpoint of theory, there is a sound mathematical justification for their use. The turning-speed combines the values of frequency and amplitude by being their product. Together with the time axis, the turning-speed curve defines the total duration of nystagmus, and delineates graphically the territory which expresses the total turning of the respective vestibular reaction. Consequently, the turning-speed curve represents a graphically expressed quantity which combines all other nystagmus quantities. The total number of nystagmus beats is the only factor which shows no direct relation to the turning-speed values, but only to the total turning; this exception is without significance, since this factor has seldom
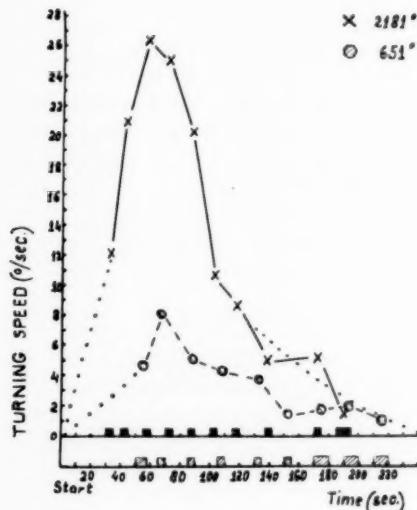
Fig. 8.—*Normal vestibulograms* for two normal persons with marked difference of response. (a) x——x: M.D., 55, operator; total turning: 2181 degrees. (b) o - - - o: Ch.S., 36, trained air force pilot; total turning: 651 degrees. The time axis is reduced to ½ of that plotted in the other figures. (Reprinted from *Trans. Am. Acad. Ophthalm. and Otolaryng.*)

been used in scientific investigations, and never for practical routine purposes.

The vestibulogram based on the turning-speed curve of a vestibular reaction represents a graph which is fairly similar to the audiogram. One of its coordinates (abscissa) contains the time factor in analogy to the frequency axis of the audiogram. The other axis (ordinate) expresses the nystagmus "intensity" as a value of turning-speed, like the decibel scale indicates the amount of hearing loss.

DEFINITION OF NORMAL VESTIBULAR REACTION

The average values obtained for normal ears are obtained from a series of normal cases comprising 40 ears, selected according to requirements described before. Of these, 24 ears were evaluated separately, because they belonged to subjects with normal ears on both sides;
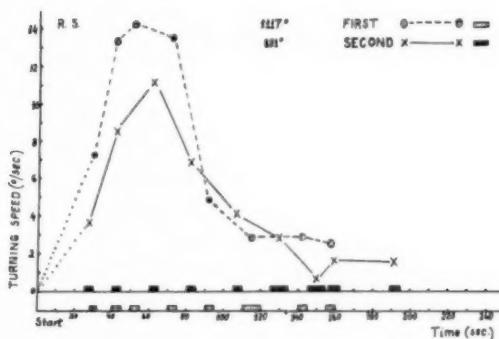
Fig. 9.—*Variations of the vestibulogram* obtained for the same ear in two different sessions one week apart (R.S. right ear). (Reprinted from *Trans. Am. Acad. Ophthalm. and Otolaryng.*)

these normal subjects consisted chiefly of hospital residents, technicians, and clerks.

After statistical evaluation, the results of our normal subjects appeared distributed over a fairly wide range. This scatter was high for the frequency and amplitude curve for reasons already discussed. The most constant results were obtained with regard to the shape of the turning-speed curve, as well as for the time factor of total nystagmus duration. As is seen in the presented figures, the total duration of the nystagmic response shows comparatively little scattering relative to the mean result. Two cases with extreme values found among normal subjects are seen in Figure 3.

Just as the routine vestibular tests of calorization and rotation produce normal results within fairly wide physiologic margins, the vestibulogram reflects a similarly wide normal range. The "intensity"-factor (turning-speed), and especially the frequency and amplitude of nystagmus, appears to be subject to various influences. In contrast, the time-factor presents more stable normal values. This is demonstrated in Figure 8 where one of the strongest reactions observed in our series (total turning 2181°) is compared to the moderate reaction of a trained air force pilot (total turning 651°).

Figure 9 shows differences measured on the same ear in two sessions one week apart. It is remarkable that a difference of similar type and proportion was observed also in the subject's other ear.

It is obvious that the vestibular apparatus may respond within fairly wide normal margins. Similar differences are known from the variable individual reactions to seasickness. In addition to this, the dissipation of temperature difference from the ear canal to the labyrinth is another variable involved.

It appears that the vestibulogram is so sensitive a recording method that it measures all physiologic variations of normal vestibular reaction. These depend on variable sustaining or inhibiting central influences as a result of differences in personality structure and emotional condition (mood, anxiety, fatigue, etc.). Moreover, vestibular reactivity may be influenced also by individual training and conditioning of the vestibular organ, such as in airplane pilots, dancers, ice skaters,[15] etc.

It is hard to classify patients with different psychologic personality structures into certain categories and to define mathematically the differences of the results obtained in such groups. However, it clearly emerged that "nervous" or emotionally unstable subjects presented higher values of turning-speed and of total turning than did those normal subjects who were known from our hospital staff as calm and relaxed personalities.

Conversely, it was interesting to note that two subjects with occupations requiring well stabilized and conditioned vestibular organs had especially low bilateral values of frequency, amplitude, and turning-speed patterns in spite of a normal total duration. One subject was an active air force pilot in steady practice, the other had been a tight-rope walker for ten years until three and one-half years before this examination. The former showed a total turning of 699° in the right ear and 651° in the left ear (Fig. 8), and the latter 184° in the right ear and 271° in the left ear.

Due to the wide range of normal responses, our results present no regular Gaussian distribution; rather, they follow distribution curves with a plateau. Therefore, the values of standard deviation and standard error of the mean do not reflect an exact expression of probability. We use them only to give an approximate impression of the scattering and for the relative comparison of the various measured factors.

In view of the wide range of normal responses, the problems of a normal reference have to be solved before abnormalities can be evaluated. Since normal persons may show different values of total

turning which depend on various intrinsic factors, an average of these values obtained from a normal population will not always serve for comparing individual results. There are normal and abnormal deviations from an average value and the patient's individual normal value (abbr. "own normal") may differ quite a bit from the average normal value.

For the evaluation of an abnormality, the determination of the patient's "own normal" reaction, i.e. the comparison of his two ears, seems to be more important than the relation of his responses to some average normal values. This situation is similar to that of difference limen evaluation in audiology, where more reliable conclusions can be drawn from comparisons with the patient's individual ability of discrimination, if obtainable, than by comparing his abnormal performance with some average normal values.[18]

At the present stage of this study, it may be assumed that a value of total turning reduced below 500° is suspected of being abnormal. Its reduction below 300° can be considered as definitely abnormal. The case of the tight-rope dancer was an exception, for already discussed reasons. Furthermore, only one other subject was found among the normals who showed with repeated investigations total turning lower than 300° in one ear without any abnormal history or findings to explain the low value and a difference between both ears.

When comparing both ears, the reduction of the total turning value in the afflicted (or worse) ear below one-half of the value measured for the good (or better) ear is also a sign of vestibular hypofunction in the afflicted ear. No interaural difference of total turning below the ratio of 0.65 was found either among the cases of bilaterally normal ears, or with repeated investigations of the same ear. Thus, an interaural difference of total turning may be normal within the range of ratios from 1.0 to 0.65.

At the present time, our intention is only to describe the range which can be considered as normal. Further details of evaluating abnormalities will be discussed in a subsequent paper.

SUMMARY

1. The pattern of various qualities of reactive nystagmus in response to a specific stimulation is investigated in 40 normal ears. The frequency, amplitude, and turning-speed curves are determined together with average normal values and normal scatter. With further

treatment of these curves, three summarizing quantities are defined: total duration, total turning of nystagmus, and total number of nystagmus beats. The method of obtaining these values through nystagmography is discussed.

2. The determined turning-speed, plotted as a function of nystagmus duration, presents a fairly stable and characteristic curve. The amplitude and frequency of nystagmus are integrated in this curve and their interdependent variations are equalized.

3. It appears that the graph of the turning-speed curve, named vestibulogram, is suitable for a simplified definition of the magnitude of any induced and spontaneous vestibular reaction. The vestibulogram describes the nystagmic response in two dimensions: a) on its time axis, the total duration of nystagmus is only one component of the vestibular reaction, b) while the height of the curve, indicating the intensity of nystagmus, seems to be an equally important trait.

4. The magnitude of any vestibular response appears to be defined by the area bounded by the turning-speed curve. This is called total turning (total amplitude). It indicates the number of degrees which would theoretically occur if the slow nystagmus component consisted of a continuous eye rotation.

5. The vestibulogram demonstrates typical curves for normal caloric reaction, the average normal values of which are discussed.

218 SECOND AVE.

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A SURGICAL APPROACH TO THE TYMPANIC PORTION OF THE FACIAL NERVE

WITH METHODS OF PRE-OPERATIVE INVESTIGATIONS

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The facial nerve pursues a longer course through a bony canal than any other nerve in the body. From the fundus of the internal auditory meatus until it emerges at the stylomastoid foramen, it traverses the rather tortuous, rigid, and snugly-fitting fallopian canal for about 35 mm of its length. Not having the support of adequate connective tissue, nor the latitude for displacement or reaction, this intrapetrous portion of the nerve is, therefore, susceptible to damage by injury or infection.

As long ago as 1908, Alt[1] performed the first recorded decompression of the facial nerve in its fallopian canal for a facial palsy of otogenous origin. Bunnell[5] accomplished the first successful intratemporal suture on the facial nerve in 1925. However, it was not until Ballance and Duel[2] presented their historic paper on the surgery of the facial nerve in 1932, that the surgical approach to this nerve came to be accepted as a standard procedure. With the introduction into this field of the binocular operating microscope and high precision instruments, the technique has been developed further. Today this operation is performed in many leading otological centers in the world as an accepted and well established surgical procedure.

Nevertheless, the horizontal (tympanic) portion of the facial nerve offers a challenge to the otologist, for it is so placed as to be almost inaccessible to the surgeon, unless he is prepared to sacrifice the ossicular chain by removing the incus. With the exception of a brief mention by Kettel,[20] a search through the literature of the past 60 years failed to reveal any work dealing with surgery of the tympanic portion of the facial nerve, except where the incus was removed. This, of course, leaves the patient with a severe conductive deafness.

It is the object of this paper to describe a technique for exposing the tympanic portion of the facial nerve, including the geniculate ganglion, without disturbing the incus. This routine was developed on cadaveric temporal bones, and there is no reason to doubt that it would be equally successful on the living subject.

SURGICAL PROCEDURE

Anatomical Considerations. The incus is stabilized in the middle ear cleft at three points, namely: 1) the fossa incudis, 2) the incudo-malleolar joint, and 3) the incudo-stapedial joint. Apart from the rather flimsy strands anchoring it in its fossa, and the two delicate joints which connect it with the malleus and the stapes, the incus, unlike the other ossicles, has no protective stabilizing ligaments. The fossa incudis, however, in spite of providing the short process of the incus with a somewhat loose and fairly shallow niche, also affords it a certain measure of protection (Figs. 1 and 2). Unfortunately, it is this short process which is the most vulnerable limb of the incus in a surgical approach to the tympanic portion of the facial nerve. However, once its position is exposed to view, and one avoids displacing or dislocating it, the short process, and therefore the incus as a whole, remains safe.

Providing the mastoid is well pneumatized, allowing an adequate working field via a posterior approach, there is sufficient room for attacking the tympanic portion of the fallopian canal in the space between the latter and the fossa incudis.

One must stress that this is an intricate operation requiring a thorough knowledge of the anatomy, and, above all, prior training on the cadaver, both to acquaint the surgeon with the anatomical approach and to provide him with the skill necessary to execute this operation. Great care must be exercised, as in addition to the risk of dislocating the incus, there is also danger of damaging the facial nerve.

Surgical Technique. The operating field is best approached through a postaural incision. The mastoid antrum is widely exposed, and the sinus plate is cleared of overlying cells. Where indicated, as in Bell's palsy, the vertical segment of the facial nerve is first exposed according to the well established method of Ballance and Duel,[2] using the binocular operating microscope, and, if no lesion is found in this portion of the nerve, one should then proceed to expose the tympanic portion. In other instances, the bend of the fallopian canal is opened just below the posterior aspect of the horizontal semicircular canal. This procedure may produce an opening into the posterior part of the

Figure 1
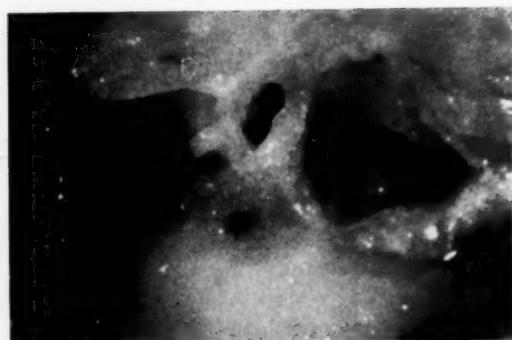
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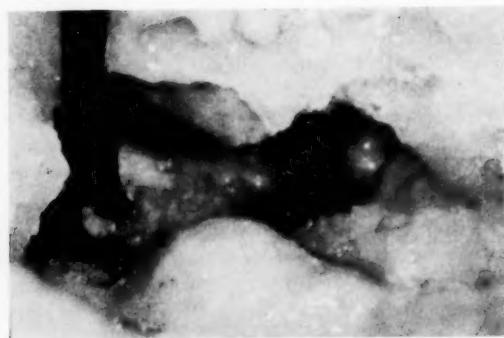
Figure 3
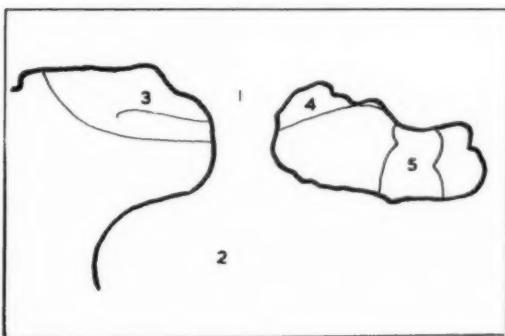
Fig. 1.—Posterior view of tympanic cavity, opened after exenteration of mastoid cells. 1) strut of bone housing the fossa incudis; 2) lateral semicircular canal; 3) short process; and 4) long process of incus; 5) stapes.
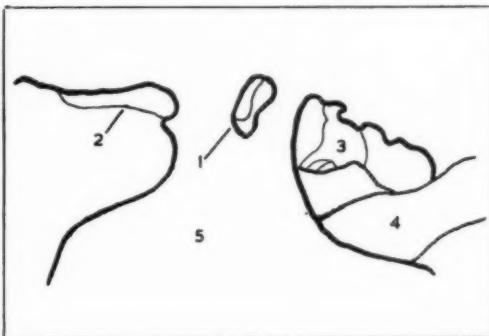
Fig. 2.—1) apex of fossa incudis exposed, housing 2) the short process of the incus; 3) stapes; 4) facial nerve; 5) lateral semicircular canal.
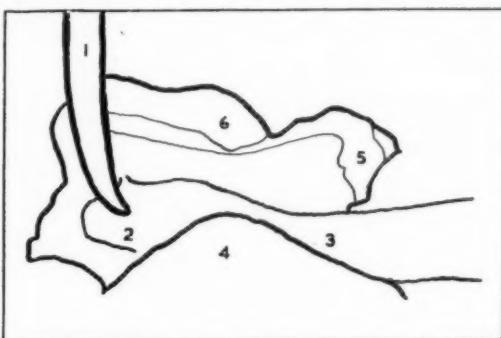
Fig. 3.—Completed operation. 1) probe points to 2) geniculate ganglion, giving off the greater superficial petrosal nerve; 3) tympanic portion of facial nerve, partly hidden by 4) convexity of lateral semicircular canal; 5) incudo-stapedial joint; 6) short process of incus.

tympanic cavity, revealing the stapes or the incudostapedial joint (Fig. 1).

The short process of the incus must now be exposed and kept in constant view. This is best done with the use of a dental diamond burr, by gradually drilling away thin layers from the strut of bone which supports the bridge and houses the fossa incudis (Fig. 2). Once the apex of the fossa incudis is opened, and the incus is identified, the latter becomes safe from disturbance, providing surgical manipulations are kept medial to the plane of the short process of the incus. The strut of bone between the incus and the lateral semicircular canal is now removed with fine short Cawthorne's gouges and flat-ended dental excavators. The tympanic portion of the fallopian canal is now seen, and, by manipulating both the patient's head and the microscope, one can follow the canal up to the geniculate ganglion.

By using fine dental probes and excavators, the thin layer of bone is lifted off the facial nerve piecemeal. This is best accomplished in progressive stages, by following the course of the nerve up to, and including, the geniculate ganglion (Fig. 3). The sheath of the nerve may now be incised, and the latter inspected.

At the conclusion of the operation small strips of prepared amniotic membrane are used to cover the exposed nerve, and the skin incision is sutured without drainage.

CONSIDERATION OF SUITABLE CASES

The only conditions which will be discussed here will be those affecting the horizontal (tympanic) portion of the facial nerve, i.e. from the geniculate ganglion to the bend posteriorly.

Bell's Palsy. It is generally agreed by Bunnell,[4] Cawthorne,[9] Collier,[10] Denny-Brown and Brenner,[11] Kettel,[20] Sullivan,[29] and others that Bell's palsy is probably due to an ischemic compression of the facial nerve within its fallopian canal, possibly caused by arteriospasm.[18] Decompression has, consequently, enjoyed its place as an accepted method of treatment for selected cases of Bell's palsy, since its introduction, in 1932, by Ballance and Duel.[2]

The site of the lesion, in the majority of cases at least, seems to be confined to the vertical portion of the facial nerve. This is outside the scope of the present paper. However, suffice it to mention that decompression of this portion of the nerve, in cases diagnosed as Bell's

palsy, does not always reveal a visible lesion. Kettel[20] found an abnormal appearance of the exposed nerve in only 80 out of the 136 cases. Cawthorne[8] has suspected this for a long time. As far back as 1936, Tumarkin[32] suggested that in the majority of cases which failed to recover after decompression, the lesion had involved the nerve in its horizontal portion; he estimated that this was the case in about 20% of all Bell's palsies. Kettel[20] quotes three cases of spontaneous peripheral facial paralysis which, at post-mortem, showed obvious involvement of the tympanic portion of the facial nerve.

Herpes Zoster Oticus. Tschiassny,[31] Tumarkin,[32] and others concluded that herpes zoster oticus produced facial paralysis by pressure on the nerve of the inflamed and swollen geniculate ganglion.

Harrison[16] found that only half the cases in his series of ten recovered completely with conservative treatment. Ballance and Duel[2] stated that, in cases in which facial palsy was assumed to be due to geniculate ganglionitis (Hunt's syndrome), a decompression was indicated, if the faradic response was persistently negative.

There are not many reported instances of geniculate herpes zoster which have been treated by decompression. Kettel[20] cites Sullivan as having operated on 17 such cases, but no results are quoted. Cawthorne,[6] however, reported decompressing a case of herpes zoster oticus with complete facial paralysis of one year's standing. He found that the nerve in the neighborhood of the geniculate ganglion was discolored and swollen. Within two months of the operation there was partial return of facial movement.

Temporal Bone Fractures. Kettel,[21] Maxwell and Magielsky,[23] and Rowbotham[26] agree that approximately 10 per cent of immediate paralyses following on head injury did not recover spontaneously, but that surgical intervention was indicated.

McHugh[24] and Ney[25] found that in longitudinal fractures of the petrous pyramid the facial nerve was most often damaged in the intratympanic portion. Cawthorne[7] traced the course of a petrous fracture with facial paralysis during a surgical exploration, demonstrating that the fracture involved the tympanic part of the fallopian canal distal to the geniculate ganglion. Similar findings were reported by Feinmesser,[14] Kettel,[21] McHugh,[24] Ney,[25] and Rowbotham.[26]

However, the middle ear being frequently damaged in longitudinal fractures of the petrous bone, disruption of ossicular continuity

may be its accompaniment. Such cases would best be dealt with by the method advocated by McHugh[24] and Shambaugh,[28] but those, in whom the integrity of the ossicular chain is proved, should certainly be given the advantage of the above surgical procedure.

From the above discussion one feels that there are indications for decompressing the tympanic portion of the facial nerve in certain cases of Bell's palsy, herpes zoster oticus, and longitudinal fractures of the petrous bone. The desire to do so has often arisen. The uncertainty of effecting a cure at the risk of inflicting the additional handicap of deafness has, however, stayed many an otologist's hand.

PRE-OPERATIVE ASSESSMENT OF SUITABLE CASES

In our clinical experience at the National Hospital for Nervous Diseases, cases of peripheral facial paralysis are investigated by taking a careful history, after which a full otological and a neurological examination is carried out, and an attempt is made to localize the lesion along the course of the facial nerve. To do this we employ quantitative lacrimation, gustation, and salivation tests, based on the topographical classification of Erb,[13] elaborated by Tschiassny.[31] As these bear a rather important relation to the surgical technique advocated above, and, as their descriptions are somewhat conspicuously absent from recent otological literature, these methods will be dealt with in some detail. In addition, certain further relevant investigations are carried out, as elaborated below.

Lacrimation Test. Epiphora in facial paralysis is not conclusive evidence that the geniculate ganglion is not involved in the lesion. The apparent increase in lacrimation may be due to any one, or a combination, of the following factors: 1) paralysis of the lacrimal portion of the orbicularis oculi muscle; 2) the falling away of the lower punctum from its normal position in contact with the eyeball; 3) sagging of the lower lid, thus forming a trough for the accumulation of tears, and their consequent spilling on moving the eyes or the head. It is, therefore, important to determine the absolute secretion of tears from the affected eye and to compare it with the contralateral side.

We apply Cawthorne's[8] modification of Schirmer's[27] lacrimation test. The patient is seated opposite the examiner and, if necessary, he is asked to dry his eyes with a piece of gauze. A piece of Whatman's No. 41 filter paper, 50 mm by 10 mm, is used for each eye. One end of the strip is folded over for about 5 mm and, with the

aid of the bent piece, the strip is hooked over the margin of the lower lid, between its outer and middle thirds. Having previously been warned, the patient is now asked to take a deep sniff from a bottle of strong ammonia (Liq. ammon. fort., B.P.), preferably through the naris of the affected side. The filter paper is observed for two minutes as it absorbs the tears, and the two sides are compared. Henderson and Prough[17] showed that the majority of normal persons manifest a difference of 3 mm or less in the flow of tears from each eye. Therefore, only a difference of over 3 mm should be considered as significant evidence of impaired function.

The greatest value of this test is in a unilateral paralysis. In the extremely rare instance of bilateral facial palsy, the same test may be carried out without the added stimulus of ammonia, and the amount of secretion, after an interval of five minutes, is compared with average secretions in normal patients, as recorded by de Roetth,[12] and Henderson and Prough.[17]

Gustation Test. Whether the clinical history is suggestive of involvement of the chorda tympani or not, gustation should be tested to ascertain the level of the lesion. A history of absence of taste on the anterior 2/3 of one side of the tongue is not always obtained, even where the involvement is subsequently proved. This may depend on the intelligence of the individual, but more so, on the fact that he may have a perfectly functioning contralateral side, non-involvement of the pharyngeal taste buds, as well as the complementary function of olfaction. Furthermore, a patient's statement that taste was at first lost, but has since returned, may indicate perception with the non-affected taste buds, rather than a true return of function on the affected side.

The test we employ is based on Hinchcliffe's[19] clinical quantitative gustometry. Being a test based on the patient's subjective response, the procedure is first explained, as co-operation is essential. The subject holds a gauze square under his chin, and is asked to protrude his tongue but not to withdraw it without instruction. He is then told that a solution, either sweet, sour, salty, or bitter, will be placed on his tongue, and that, as soon as he recognizes a taste different from that of water, he is to indicate this by raising his hand. If he does not perceive a taste after several seconds, the unaffected side is similarly treated as a control. Finally, he is asked to withdraw his tongue. If necessary, the test is repeated for all four substances. Using this procedure, the majority of normal individuals should be
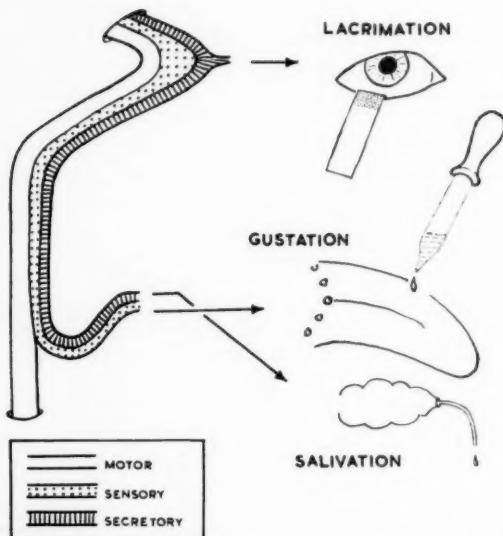
Fig. 4.—Diagrammatic representation of the physiological components of the intrapetrous part of the facial nerve, and our methods of testing their function.

able to perceive solutions of the following strengths: sucrose 8.32 gm/100 cc, tartaric acid 0.407 gm/100 cc, sodium chloride 2.00 gm/100 cc, and quinine sulphate 0.0224 gm/100 cc.

Salivation Test.   This test is not done routinely, but when in doubt regarding the function of the chorda tympani, it may be used to supplement the gustation test.   A polythene tube of 1 mm external diameter is inserted into each submandibular salivary duct.   The patient is given a lemon-flavored boiled sweet to suck, and is asked not to bring his teeth together, as he may bite the tubing.   The amount of salivary secretion of the two sides is compared.

Anatomical Interpretation of Tests.   Figure 4 shows diagrammatically the various components of the intrapetrous part of the facial nerve.   Please note that the suprachordal segment, i.e. that part of the nerve from the geniculate ganglion to the level of origin of the chorda tympani, includes the intratympanic portion of the facial nerve.

TABLE I

TOPOGRAPHICAL LEVEL	LACRIMATION	TASTE	SALIVATION
Geniculate	Diminished	Absent	Diminished or Absent
Suprachordal	Unaffected	Absent	Diminished or Absent
Infrachordal	Unaffected	Unaffected	Unaffected

Table I summarizes the findings for lesions at the various levels of the facial nerve within the fallopian canal.

Tschiassny[31] pointed out that the above method of localizing the lesion is only valid in early paralyses. In lesions of some standing, partial recovery may have taken place in fibers of a particular function, e.g. in a lesion of the geniculate ganglion, lacrimation may return without an obvious improvement in the paralysis. These tests, therefore, serve merely as a guide to locating the lesion.

Electrical Testing of Lower Motor Neuron. Electrical testing in facial paralysis resolves itself into two main aspects, namely: 1) determination of intensity-duration curves, and 2) electromyography.

The old established galvanic and faradic tests are essentially determinations, at discrete points, on the intensity-duration curve. They have, therefore, been superseded by this more extensive quantitative measurement.

While it is not proposed here to enter into the complicated aspects of electrical tests of nerve and muscle function, it is useful to mention the value that these tests can have with respect to facial paralysis. Both electromyography and strength-duration curves can indicate degeneration of the lower motor neuron. Consequently, these tests can separate lower motor neuron palsies into those with conductive block only, and those in which there is nerve degeneration. This differentiation is very important from a prognostic point of view. Taverner[30] found that all cases of Bell's palsy, where the paralysis was due solely to a conductive block, recovered spontaneously and completely. It is to be noted, however, that in Bell's palsy nerve degeneration will only reveal itself electrically at least a fortnight after the onset of the paralysis.[15]

In head injuries with immediate facial paralysis, where a very severe injury to the facial nerve may be suspected, electromyography

enables us to establish earlier evidence of nerve degeneration. Gilliatt and Taylor,[15] after studying the electromyographic responses in patients with complete operative section of the facial nerve, concluded that evidence of degeneration can be expected on the fourth day after section.

Radiography. There is no need to stress the importance of good radiographs in cases of head injury with facial paralysis. Maxwell and Magielsky[23] point out, however, that there is general agreement, that such a paralysis in acute head trauma indicates a temporal bone fracture in nearly every case.

Good pneumatization of the mastoid bone should be established pre-operatively, as this is an essential prerequisite for the operation described above. Fortunately, it is extremely rare to find a case of Bell's palsy with a poorly pneumatized mastoid bone.

Audiometry. In head injuries with facial paralysis, in addition to tuning fork tests, repeated pure tone audiograms, for air and bone conduction, should be performed at intervals, to establish the integrity of the ossicular chain. If a persistent conductive loss is present, suggesting disruption of the ossicles, our operative procedure is not indicated, but a hemotympanum should first be excluded.

It is, nevertheless, advisable to have a pre-operative audiometric record of the patient's hearing in all cases which are to undergo decompression of the horizontal segment of the facial nerve.

In addition to the above investigations, when indicated, the patient may be subjected to further tests of labyrinthine function, such as elicitation of caloric-induced and optomotor nystagmus.

COMMENT AND CONCLUSIONS

There has long been the need for a sound surgical approach to the tympanic segment of the facial nerve in certain cases of Bell's palsy, geniculate herpes zoster, and in longitudinal fractures of the petrous bone. Behrman,[3] Cawthorne,[9] Kettel,[21,22] Maxwell and Magielsky,[23] McHugh,[24] Ney,[25] Rowbotham,[26] and others have repeatedly stressed the importance of surgical decompression in such cases of peripheral facial palsy, where the lesion is *surgically accessible.*

The present day concept is that the vertical portion of the facial nerve is accessible in trained and experienced hands. It is, relatively, not an infrequent procedure in many modern otological centers.

The tympanic portion of the facial nerve, however, has in the past been accessible only at the expense of the integrity of the ossicular chain of the middle ear. Kettel[20] mentions having exposed this part of the nerve right up to the geniculate ganglion, but, apart from this, there has been no definite attempt at tackling this problem. The reason for this is obvious: where a possible lesion of the horizontal segment of the facial nerve confronts the otologist in a patient with an intact ossicular chain, disruption of the sound conducting apparatus, by removing the incus, in order to render that part of the nerve surgically accessible, is not justifiable, because a full return of facial function cannot always be reasonably expected. It would be quite unjust to inflict a further social handicap on the unfortunate patient. If, on the other hand, the facial nerve could be exposed up to the geniculate ganglion, without disrupting the ossicles, then, at least, the patient has lost nothing, while being given a better chance of recovery.

The author believes that in Bell's palsy, even where pre-operative examination precludes the involvement of the greater superficial petrosal nerve, if, after exposing the vertical segment, no obvious lesion is detected, the patient ought to be given the benefit of decompression up to the geniculate ganglion. Cawthorne[8] has found that, in practically all the Bell's palsies which showed no obvious lesion at decompression of the vertical part of the facial nerve, there had been pre-operative decrease of lacrimation on the affected side. In these cases he postulates the possibility of the lesion being situated more proximally, probably in the region of the geniculate ganglion.

In herpes zoster oticus, and in longitudinal fractures of the petrous bone with facial paralysis, only the tympanic portion and the geniculate ganglion need be exposed by the method described above, which makes this region surgically accessible in the majority of cases.

It is hoped to follow up this paper with a supplementary report of cases which have undergone the operative treatment described in this paper.

SUMMARY

A technique is described for exposing the whole length of the tympanic portion of the facial nerve right up to, and including, the geniculate ganglion, without disrupting the incus, thus making this segment of the nerve surgically accessible. The indications are discussed for performing this operation in Bell's palsy, herpes zoster

206   *LESLIE BERNSTEIN*

oticus, and longitudinal fractures of the petrous bone.   Clinical methods for localizing the lesion are presented.

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PECULIARITIES OF NOISE-INDUCED
HEARING LOSS

A STUDY OF THE HEARING LOSS
OF ENGINE-ROOM PERSONNEL

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For industrial workers who are exposed to noise the data on sound pressure level (SPL) and exposure duration usually cannot be evaluated with exactitude. In most cases these workers are not continuously employed during the entire work-time in a space where a constant SPL is present. In the marine engine-rooms personnel we believe we have found a group where the above data are more accurately known. For during a specific part of the day this personnel is continuously present in a room with a practically constant noise level. A study of the hearing threshold in this group may give us a clearer insight into the peculiarities of noise-induced hearing loss.

With the arrival of Diesel engine and steam turbine as propulsive power of vessels a SPL has been established in the engine-rooms of these vessels which is injurious to the auditory organ. Thus de Wit[1] finds in 10 corporal-engineers of submarines a hearing loss at 4096 cps averaging 32 db. This considerable hearing loss is understandable since Lund-Iversen[2] measures 100-112 db as the highest SPL in the engine-rooms of submarines; in those of motor-torpedo boats this amounts to as much as 102-124 db according to the number of revolutions of the engine. In view of such high values it does seem surprising that the latter author finds a trauma in only one-fourth of the engine-room personnel; however, he does not state what criterion was chosen for the threshold shift.

For engineers of naval vessels Gravendeel[3] finds an average hearing loss that is larger than can be expected by reason of age. The above-mentioned publications relate to naval craft, viz. comparatively small ships provided with very powerful engines. However, Baron, Carré

and Lebec[4] also find a high SPL on merchant vessels with, as a conse-
quence, nearly always a threshold shift at 4096 cps in the engine-room
personnel.

In Figure 1 an instance is given of the SPL's as they may occur
on a vessel. The SPL has been registered for various octave-bands;
this is of importance because the traumatizing capacity of sound is
among other things dependent on the frequency spectrum. The SPL
of an old-fashioned steam-piston engine, now practically out of use,
is distinctly lower than that of the modern steam turbine and Diesel
engine; the illustration shows that the SPL of a steam-piston engine
is only just below the critical level of 50 sones per octave band pro-
posed by Hardy.[5] However, the SPL of steam turbine and Diesel
engine lies clearly above this criterion. The auxiliary engines put up
in the engine-room, too, produce a SPL exceeding Hardy's criterion.
Carré and Lebec[6] measure over-all SPL's of 104-117 db at 50 cms
distance from the auxiliary engine-group; in the frequency range of
1600-6400 cps the SPL amounts to 93-106 db. On the ground of
these measurements it can be expected that employment in an engine-
room where above SPL's are prevalent will result in an impairment of
the inner ear after a certain time.

The SPL outside the engine-room proves to be considerably lower
(Fig. 1). Frequently the over-all level is still fairly high, but this
sound-pressure is chiefly caused by the rather harmless frequencies
below 400 cps and is there also below Hardy's critical level. So the
deckcrew is not exposed to traumatizing noise.

METHOD OF INVESTIGATION

The hearing threshold for pure tones of deck- and engine-room
personnel was investigated. Beforehand an otological history was
taken and an otoscopic examination made. Further the periods of sea-
service of each individual were closely copied from the seaman's book.
Persons with an otoscopic defect pointing to an upset in the conduc-
tion mechanism were left out of consideration. The investigation was
made in the period when a ship was staying in the home port. The
hearing threshold was determined in a room situated in a cellar the
walls of which are hung with blankets. The level of background
noise measured in this room is so low that according to Cox's criterion[7]
the zero db threshold can be duly determined (Fig. 2).

The tone threshold audiogram was taken with a continuous audi-
ometer constructed according to Van Dishoeck's[8] system, make Peekel,
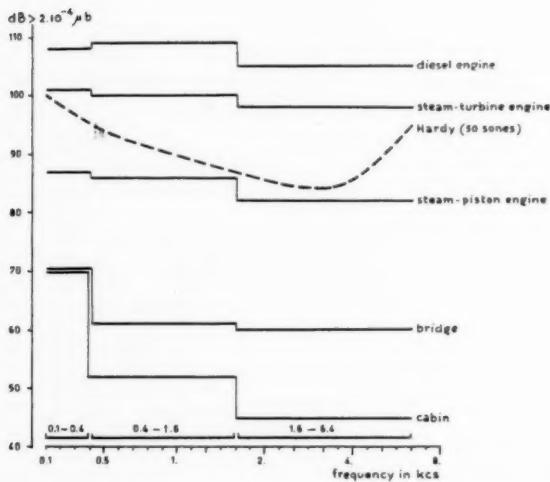
Fig. 1.—Illustration of the SPL's as they may occur on board seagoing vessels. The critical level according to Hardy (50 sones per octave band) roughly marks the boundary between the traumatizing and non-traumatizing noise spectrum (after Carré and Lebec).

type D 4. It is adjusted to various sound levels (in 5-db steps) and the threshold of hearing is determined by varying the frequency (this is continuously possible from 80 to 10,000 cps). The value of this method has been proved especially for the noise-induced hearing loss, because in the initial stage slight dips will often occur which are only partly or not at all perceptible with octave audiometry. Mostly the determination of the air conduction audiogram would suffice. When at 1000 cps a distinct loss in air conduction was present a bone conduction audiogram was taken as well so as to rule out any conduction loss.

For the purpose of calibration threshold audiograms of 20 normal control ears were taken in the testing room and the median curve of these was computed. The zero db level of the audiometer was calibrated by means of a 6 cc artificial ear. The curve in Figure 3 represents the calibration curve of the audiometer in which the found median curve of normal ears was incorporated. By way of comparison the normal threshold curve according to Dadson and King[9] (for octave audiometry) was also drawn in. Above 1000 cps there proves to be little difference between the two curves, below around 750 cps
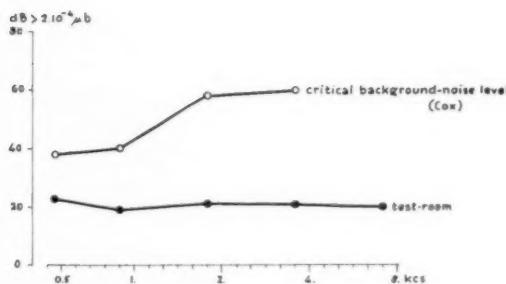
Fig. 2.—The curve marked ●———● represents the SPL in the testing room. The o———o curve is the lowest allowable level of background noise at which, according to Cox, zero db loss is measurable.

the curve of Dadson and King is distinctly on a lower level. Van Leeuwen,[10] who also uses a continuous audiometer for his researches, has the same findings. The difference between the curves in the frequency range below around 750 cps is probably due to the difference in method of threshold determination.

ANALYSIS OF THE THRESHOLD CURVES

Glorig[11] has pointed out the occurrence of threshold shifts, identical with those at noise-induced hearing loss, in persons not employed in a noisy environment. He calls this sociocusis. In this connection Gravendeel and Plomp[12] speak of micro noise trauma. In order to trace whether the threshold shift is occupational, comparable groups each consisting of 36 subjects were selected from deck- and engine-room personnel. The group of deck-personnel may be considered to be only affected by sociocusis and forms a safe comparison for the determination of the actual occupational trauma of engine-room personnel. The age of the groups averages 23.08 and 24.95 years and the length of sea-service 66.8 and 58.2 months for deck- and engine-room personnel respectively. The now following calculation has been based on the maximal threshold shift above 1000 cps; this has proved a good standard for the amount of dip-shaped hearing loss (Plomp and co-workers[13]). The average maximal threshold shift found for the group of deck personnel was 12.6 db and for the group of engine-room personnel 26.1 db. This difference is statistically significant (p between 0.01 and 0.001). From this it follows that the high sound level in the engine-room induces a significant threshold shift.
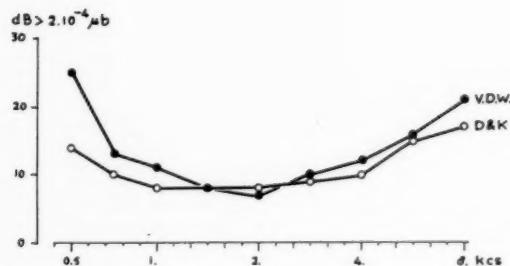
Fig. 3.—The curve marked ●————● represents the calibration curve of the audiometer, measured with an artificial ear, in which the median threshold curve of a group of persons of normal hearing has been incorporated. For comparison the normal curve of Dadson and King was entered (○————○).

For eight hours a day the engine-room personnel are occupied in the engine-room. The period between departure and arrival in the home port is always taken as exposure duration. During the time spent in overseas ports (this amounts to about 60 per cent of the total length of voyage) only the auxiliary engines are operating, which, as was discussed before, also produce a high SPL in the engine-room. Thus the exact exposure duration can be figured out in engine-room hours, just as is done in flying hours in the case of airmen. One year's sailing corresponds to slightly less than 3000 engine-room hours.

Like noise-induced hearing loss presbycusis also causes a perception loss in the high tone area. This factor was taken into account by discounting this loss in the audiograms of persons over 30 years by simple subtraction of the physiological threshold shift to be expected, which would be justified according to the investigations of Motta and Profazio.[14] The values as stated by Jatho and Heck[15] were incorporated in Table I. The subtraction of these values has been applied in all subsequent calculations.

To render an accurate reading of the threshold shift possible in a particular frequency area of the continuous audiogram the tone-scale was divided into a number of bands (Van der Waal[16]). From 1000-8000 cps a logarithmic scale of base 2 was utilized. Each octave was again subdivided into 6 bands; from 1000-8000 cps 18 bands are thus obtained, each comprising 1/6 octave. Below 1000 cps a linear scale was adopted; up to 400 cps 6 bands are obtained each 100 cps large;

TABLE I

THE PHYSIOLOGICAL THRESHOLD SHIFT IN DB WITH INCREASING
AGE (PRESBYCUSIS) WITH RESPECT TO THE HEARING THRESHOLD
AT 21 - 30 YEARS as incorporated in the audiograms used in the present study
(after Jatho and Heck)

	1.8	2	2.2	2.5	2.8	3.2	3.6	4	4.5	5	5.6	6.4	7.2	8	kcs.
31-40 years	5	5	5	5	5	5	5	5	5	5	10	10	5		
41-50 years	5	5	5	10	10	10	10	10	10	10	15	15	20		
51-60 years	5	10	10	15	15	20	20	20	20	25	25	30	35		

these are here as large as the 900-1000 cps band would be on the loga-
rithmic scale. In this manner the frequency range of 400-8000 cps
contains 24 bands, on the scale equally large. This division into a
logarithmic and a linear part was first indicated by Koenig[17] for use
in psycho-acoustic data. Davis and co-workers[18] and Schuknecht[19]
used this scale in experiments concerning the auditory organs of guinea
pigs and cats respectively. They call it the anatomical frequency scale
because in it the functional and pathological changes of the cochlea
are in linear correspondence.

Out of 234 threshold curves of 117 persons from the engine-room
197 curves of 107 persons reveal a threshold shift of 15 db or more
in the frequency range of 1000-8000 cps. The frequency band con-
taining the center of the largest threshold shift was registered for each
ear and plotted in a histogram (Fig. 4). With the majority of the
curves, namely, in 69%, the center of the threshold shift lies between
3600 and 5600 cps. In a few audiograms it is below 3000 cps; this
occurs at threshold shifts extending to the lower frequencies like those
found in severe as well as in initial noise-induced impairments.

In Figure 4 we saw that the site of the threshold shift in the
frequency range is not the same for different individuals. When
computing the median curve of a group of audiograms this factor
is ignored. For the median is determined independently of the indi-
vidual differences as to the localization of the threshold shift. In this
way the character of the separate curves is for the greater part lost.
The separate curves will be much more pronounced when the fre-
quency bands with the center of the greatest loss are placed below
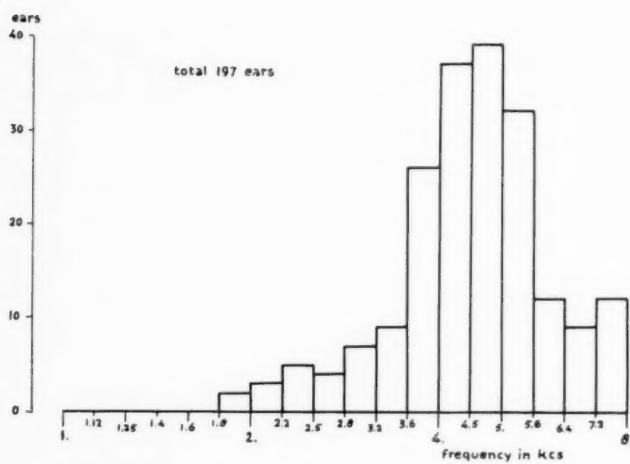
Fig. 4.—The distribution of the largest threshold shift in the frequency area of 1000 to 8000 cps. On the base the frequency has been plotted in bands of 1/6 octave; on the ordinate the number of threshold curves. For each ear with a threshold shift the frequency band with the greatest loss has been set out.

each other and the median is determined next. The result is then a median-dip. As a consequence there is no longer any information on the localization of the threshold shift in the frequency range. As frequency band in which the maximum of the median-dip has been recorded the median of the frequencies containing the maxima of the separate dips is taken. This method of operation has practical advantages because pattern and amount of the threshold shift are shown off better in a group. This is well illustrated by Figures 5 and 6. In Figure 5 the threshold curves are divided according to the depth of the dip into 4 groups: 15-30, 35-50, 55-70 and more than 70 db threshold shift. Of the area comprising one and one-half octaves with the largest threshold shift in the center the median for each group of threshold curves was represented. This median dip was marked down on the tone scale where most of the separate dips occur. In each of the groups a distinct dip-shaped curve is found, steepest in the groups with a moderate loss. The figure also shows that at a slight threshold shift the maximum is lower in frequency. In the curve of 70 db or more loss the threshold in the frequency range above the lowest point of the curve is more increased than below it. There is a
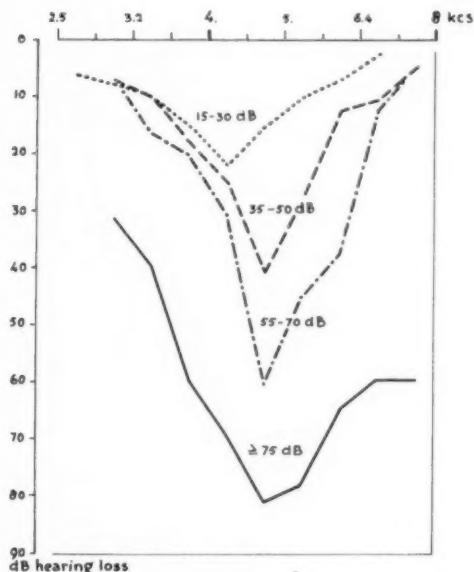
Fig. 5.—The median dip represented for the groups with a largest loss
of 15-30, 35-50, 55-70 and more than 70 db respectively.   On the abscissa
the frequency has been plotted in kcs, on the ordinate the threshold shift
in db.

tendency to a more sloping curve as described in advanced stages of
noise impairment.   Figure 6 represents the median curve of the entire
material; it is uncorrected for presbycusis so that comparison with
curves from the literature is possible.   The median curve of the area
with the greatest hearing loss, the median dip, has been corrected for
presbycusis.   The median of the control group has been drawn in as
well.   The median dip clearly shows that there is mostly a sharp dip-
shaped loss, and that the largest number of dips is localized round
5000 cps.   The figure clearly illustrates that this median dip affords a
better insight into the threshold shift as regards pattern and amount
than the median threshold curve.

It is generally known that there exists an individual susceptibility
to sound.   Van Leeuwen[10] among others demonstrates this for the
experimental tone-dip.   On exposing 108 ears for 3 minutes to a tone
of 2800 cps, 100 db, he finds differences in the maximal hearing thresh-
old shift of 0-30 db (median 7 db); 24% of the ears is found to
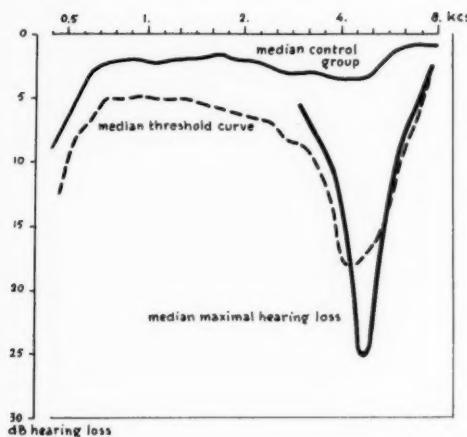
Fig. 6.—The median threshold curve of the engine room personnel under examination (334 audiograms) is uncorrected for presbycusis. The median-dip (median of the maximal hearing loss) has been corrected for presbycusis. Further the median of the control group of normal hearing persons has been drawn in. On the abscissa the frequency has been plotted in kcs, on the ordinate the threshold shift in db.

be insensitive and 13% highly sensitive. Our material is eminently suitable for the study of this interesting problem concerning noise exposure. For this purpose the audiograms of 24 subjects were selected out of the 18-29 age-group, whose exposure duration to engine-room noise was about uniform: round 3 years (2-4 years); figured out in engine-room hours this is round 9000 hours. The highest threshold shift was recorded separately for left and right ear. From the relative histograms (Fig. 7) it appears that a threshold shift of 20-30 db is most common, but in less than half of the total number. Broadly speaking there is no clear difference between the diagrams of left and right ear; however, as will be discussed below in greater detail, differences between the ears of one and the same individual are often present. The above results prove that just as at subjection to pure tones there is also a distinct individual difference in susceptibility to a complex sound such as engine-room noise.

Figure 8 shows us the difference in amount and localization of the threshold shift in left and right ear of the same subject. Histogram 8A represents the individual difference in amount of the thresh-
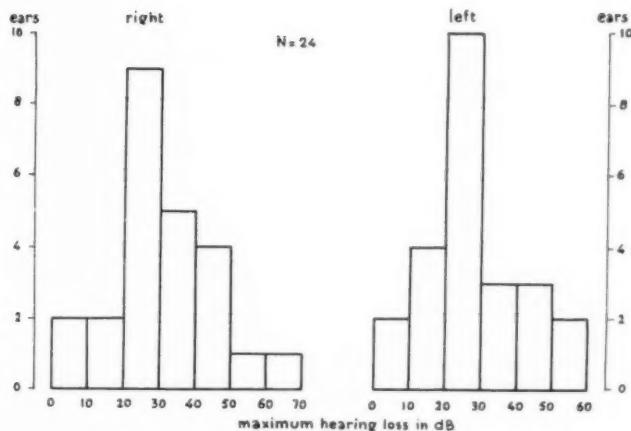
Fig. 7.—The maximal threshold shift of 24 persons between 18 and 29 years with an about equal exposure duration to engine room noise (round 9000 engine room hours), represented for the right and left ear separately. On the base the threshold shift has been plotted in 10 db steps, on the ordinate the number of ears.

old shift at one or both ears. The 107 subjects with a threshold shift at one or both ears group themselves about symmetrically round the group with an equal loss right and left. That there are exceptional cases is evidenced by the subject whose left ear is damaged 90 db more than the right ear. Histogram 8B marks the difference in localization of the threshold shift of the left ear as regards the right ear of the same individual. Ninety persons in total display a threshold shift at both ears. The threshold shift left and right proves to be found mostly in the same frequency range, for two-thirds of the total number within one-half octave. For 35 persons the threshold shift of the left ear is lower, for 22 persons higher in the frequency range as compared with the right ear. However, statistically seen this difference may be accidental.

What relation is there between the progression of the threshold shift and the exposure duration? On this important problem, too, the material is informative. Figure 9 represents the median of the maximal threshold shift for groups with different exposure duration, once more with the aid of a histogram. The exposure duration has been marked on a logarithmic scale (except for the 0-6 months
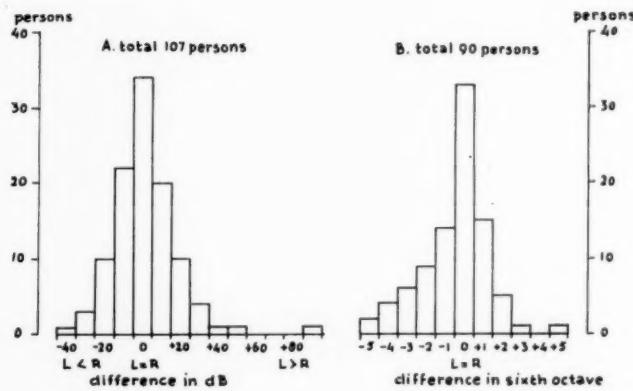
Fig. 8.—The difference in threshold shift between left and right ear of one and the same person.

In histogram A the individual difference in amount of the maximal threshold shift between left and right ear has been represented. On the base this difference has been plotted in 10 db steps, on the ordinate the number of persons has been set out. At "0" on the base the number of persons has been plotted in whom the greatest loss at the left is equally large as at the right ear, at "+20" on the base the left ear is damaged 20 db more than the right ear, etc.

In histogram B the individual difference in localization of the maximal threshold shift of the left ear as compared with the right ear has been represented. On the base this difference in localization has been plotted in frequency bands of 1/6 octave, the ordinate indicates the number of subjects. At "0" on the base the number of subjects is found in whom the maximal damage left and right is situated in the same frequency band, at "+1" this is 1/6 octave higher in frequency at the left than at the right ear, etc.

group). On exposure of 1 to 8 years there proves to be little difference in threshold shift; in other words, the definite trauma is sustained practically in the very first year. Van Leeuwen[10] has the same findings regarding employees of shipyards; Gravendeel[3] establishes the greatest increase in hearing loss of naval engineers also during the first years of exposure.

On 8-16 years of exposure the threshold is once more seen to increase (Fig. 9). From the above we may conclude that within a short time the engine-room noise induces a threshold shift which reaches a given maximum in the very first year. After about 8-16 years of exposure the threshold shift increases once again, in spite of
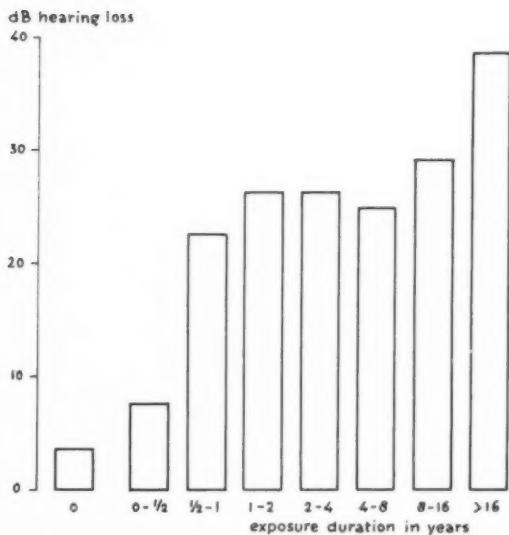
Fig. 9.—The median of the maximal threshold shift has been plotted in a histogram as a function of the exposure duration. On the abscissa the exposure duration to engine room noise has been plotted on a logarithmic scale (except for the group 0-6 months); on the ordinate the median of the largest threshold shift has been designated in db. At "0" on the abscissa the threshold shift of the control group of persons of normal hearing has been drawn in.

the correction for presbycusis. This second increase will be discussed in greater detail in a subsequent study on presbycusis.

The frequency-range of 500-2000 cps is the most important one for the hearing of conversational voice. On the strength of this, rules were drawn up by the Subcommittee on Noise of the American Academy of Ophthalmology and Otology[20] concerning the computation of the percentage hearing impairment. When between 500 and 2000 cps the average threshold shift does not exceed more than 15 db at one or both ears, there are decidedly no difficulties to be expected in everyday speech; the hearing impairment is then 0%. When the average hearing threshold between 500 and 2000 cps amounts to 82 db or more, the above-mentioned Subcommittee fixes the hearing impairment at 100%. For calculation of the binaural hearing impairment the following formula is given: five times the percentage of the

TABLE II

ENGINE-ROOM PERSONNEL WITH A HEARING IMPAIRMENT
According to the Criteria of the *Subcommittee on Noise of the American Academy of Ophthalmology and Otology* (13 persons out of 117)
The corresponding values of the percentage hearing impairment,
the exposure duration and the age have been designated.

PERCENTAGE HEARING IMPAIRMENT	EXPOSURE DURATION IN MONTHS	AGE IN YEARS
2½	12	39
2½	168	36
4	96	31
5	60	25
5½	336	54
6	36	27
6½	36	23
7	180	48
12	360	57
15	360	59
18½	468	55
32	313	53
39	420	59

better ear plus the percentage of the worse ear divided by six. The following computations are based on the threshold values without correction for presbycusis. Of the engine-room personnel 104 out of the 117 subjects prove to meet the criterion of an average hearing loss of less than 15 db between 500 and 2000 cps at both ears (hearing impairment 0%); so 89% has no hearing loss in the frequency range important for speech intelligibility. When the threshold shift of 500-2000 cps lies between 15 and 30 db (hearing impairment 0 - around 22½%) there are no handicaps in the ability to understand ordinary voice, but there are for low voice. Eleven persons fall into this group. Only 2 subjects can be expected to have minor difficulties with conversational speech; their hearing impairment amounts to 32 and 39%. They prove indeed to be somewhat handicapped for ordinary voice, but loud voice is readily understood.

In conclusion it can be said that 98% of the engine-room personnel under examination has a normal or nearly normal hearing for speech; only 2% has some difficulties in following conversational speech.

In Table II the percentage hearing impairment, the exposure duration and the age of the subjects have been set down side by side. It appears that a hearing impairment of 10% and more occurs exclusively in persons over 50 years and on an exposure duration of 25 years or more.

COMMENT AND SUMMARY

From sound measurements in the engine-rooms of seagoing vessels it appears that the noise level prevalent there is injurious to the auditory organ. The resulting trauma depends on the individual susceptibility, however. Threshold audiograms of engine-room personnel show that 91% has a threshold shift of 15 db or more. The noise to which the deck personnel is exposed lies below the harmful level. Consequently comparison of the threshold audiograms of a comparable group of deck- and engine-room personnel shows a significant difference in threshold shift.

Closer analysis of the threshold audiograms of the engine-room personnel proves that there are differences between the ears of different persons as well as between the two ears of one and the same person as regards the degree of threshold shift and the localization in the frequency range. The difference in amount of hearing loss between left and right ear was found to be not significant; this in contrast with inner ear impairment caused by shooting with rifle, pistol, machine-gun, etc., where the left ear is damaged more significantly owing to the left ear being directed forward.[21]

The threshold shift of the engine-room personnel examined proves to increase not proportionally to the exposure duration of the noise. Fairly rapidly (in our material within 12 months) a particular threshold shift is reached which hardly shows any further increase during the next years. After an exposure of 8-16 years a slight increase in threshold shift is once more perceptible.

Ultimately the hearing loss for everyday speech is the most important factor, however. This is chiefly dependent on the threshold in the frequency range of 500-2000 cps. On this basis the percentage hearing impairment was calculated. Two persons are moderately handicapped in conversation; they have worked in engine-rooms for over 25 years and in addition are older than 50 years. In general, the hearing impairment at the end of working life will be rarely sufficiently serious as to render normal conversation impossible.

This does not alter the fact that from a preventive point of view the described threshold shift should be kept as small as possible. Moreover working in noise is psychically objectionable. The wearing of earplugs or ear-muffs is often inapplicable because the temperature in the engine-room is too high; this will be particularly the case when sailing in the tropics. It will be better to reduce the SPL in the engine-room. This problem is already receiving the attention of marine construction engineers.

Further it will be advisable to eliminate persons with ears sensitive to noise at an early date, before severe irreversible impairment has been inflicted on the inner ear. For this purpose a pre-employment audiogram with a follow-up within 12 months will be necessary (Fig. 9). Which individuals should be eliminated on the strength of these will depend on several factors, a.o. on the possible hearing loss revealed by the pre-employment audiogram and also on age. Each case will have to be judged individually; no hard and fast rules can be laid down with the data known at present.

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XVII

THE LATERALIZATION METHOD
FOR EVALUATING
MONAURAL DEAFNESS

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In 1958, the author presented a preliminary description of a new method for verifying the presence of residual hearing in cases of monaural deafness. Basically the method involves four separate measurements: the puretone air conduction shadow curve (shadowgram), the lateralized speech reception threshold (Lat-SRT), a lateralized speech discrimination score (Lat-PB) using the standardized PB words, and a voice quality report. The method has several quantitative advantages. Foremost among these features is the fact that no masking is required, thus eliminating certain variables. Furthermore, it is almost impossible to malinger successfully all of the measurements employed since the stimuli are transmitted across the skull and the subject cannot rely readily upon his previous auditory experiences which were acquired primarily through the air conduction pathway. In addition to verifying the presence of monaural deafness and estimating the extent of the non-organic loss, if any, the response integrity of the subject may be evaluated.

CLINICAL DATA

From our case files, we find that monaural deafness occurs in about one out of five cases. Added to the battery of functional hearing tests for monaural deafness, the lateralization method has proven to be extremely valuable. If the monaurally deaf patient is able and willing to co-operate, then he will pass the four criteria and the validity of our clinical results is enhanced. If he is unable or unwilling to co-operate, he will fail one or more of the four measurements in the method. Each of the criteria will be discussed separately. We have collected 60 cases of monaural hearing loss for discussion.

Shadowgram. We prefer to use the term shadowgram for the lateralized, puretone, air conduction shadow curve. A minimum of seven thresholds are determined using an ascension to threshold ap-

proach. Four to five ascension series are made and the lowest, modal response taken as the threshold. The seven test frequencies are 1000, 2000, 4000, 8000, 500, 250, and 125 cycles.

The shadowgram should parallel the puretone, air conduction thresholds in the better ear. The two curves will generally be separated by an average of 50 db $\pm$ 5. Allowance must be made for individual differences in the size, shape, mass and elasticity of the skull. At the present time, these variables have not been fully evaluated. A more important factor is the response reliability and integrity of the patient. The shape, level and response reliability of the shadowgram are the important considerations. The average of the three central frequencies (500, 1000, and 2000 cycles) of the shadow curve is computed for comparison with the lateralized speech threshold. The clinician should not make the mistake of using audiometric zero to compute the level of the shadowgram. It is the difference between the two audiometric curves which is computed.

Lateralized SRT. This measure should agree with the mean of the three frequencies, 500, 1000, and 2000 cycles of the shadowgram within $\pm$ 5 db; depending, of course, on the shape of the audiometric pattern. A flat loss will correspond more closely with the Lateralized SRT than will a sharply falling loss in the higher frequencies. The Lateralized SRT is obtained and the difference between the SRT for the better ear is subtracted from it so that this score will always be on the order of 50 db. We found that the Lat-SRT ranged from 45 to 60 db with a mean of 52 db and at the same time was in agreement with the level of the three shadow curve thresholds. It is obtained by the usual psychophysical procedure.

Lateralized PB Score. The 50 words are presented by monitored live voice at a level 15 db above the Lateralized SRT. To this score is added the PB loss in the better ear so that the expected PB score will always be on the order of 50%. For example, if the Lateralized PB score is 40% and the PB decrement in the better ear is 4%, then the total score for the lateralized measure is 40 + 4 or 44%. The observed scores ranged from 40 to 60% with a mean of 50% in our standardization group. The clinician should seek an explanation for a score that is too high or too low. The latter is usually indicative of poor co-operation while the former is usually indicative of binaural perception.

Voice Quality Report. This information is solicited after the Lateralized PB score is obtained and at the same audiometric level. The patient with a deaf ear who is responding correctly will most often

Name S.W.   Age 38   Date 6-16-59
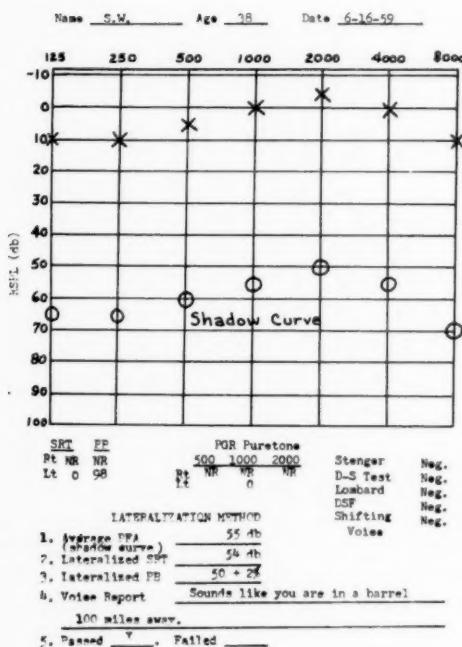
Fig. 1   Case 1

comment that the voice sounds *faint*. This is understandable since he is hearing the speech at a sensation level of 15 db. If he has elevated his thresholds so that the lateralized stimuli are heard binaurally, he will comment usually that the speech is *clear and distinct*. This is what we would expect from binaural rather than monaural perception.

ILLUSTRATIVE CASES

This section will describe five clinical patients who were examined by the lateralization method and other auditory tests. The patients were five males with monaural hearing loss in the right ear ranging from 20 db to total deafness as measured by the limits of contemporary audiometry.

Figure 1 is the audiogram of a male, aged 38, who has a deaf right ear and a normal left ear. The functional hearing tests—Sten-

Name R.S. Age 45 Date 4-24-58

125 250 500 1000 2000 4000 8000

RSPL (db)

SRT	PB		PGR Puretone			Stenger	Pos.
Rt NR	NR		500	1000	2000	D-S Test	Neg.
Lt 10	98	Rt	60	60	60	Lombard	Pos.
		Lt	5	10	15	DSF	60 db
						Shifting Voice	60 db

LATERALIZATION METHOD
1. Average FFA _____ 62 db
2. Lateralized SRT _____ 70 db
3. Lateralized PB _____ 94 + 2%
4. Voice Report _____ Sounds very low and seems near.

5. Passed _____ . Failed X
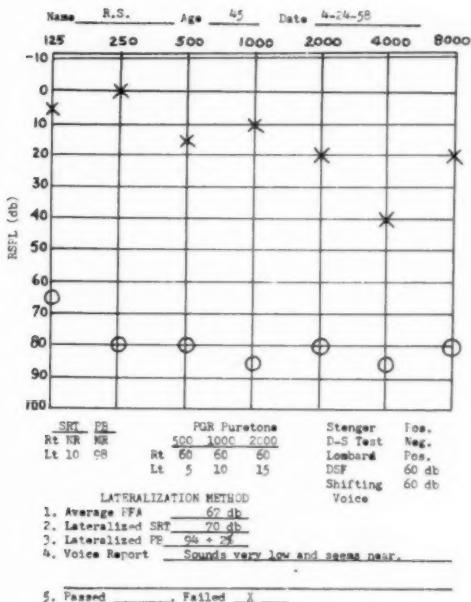
Fig. 2   Case 2

ger, Doerfler-Stewart, PGR puretone, Lombard, Delayed Speech Feed-
back and Shifting Voice—were negative. These measurements are
supported by the results of the lateralization method reported below.

CASE 1. The puretone shadowgram is normal as to shape, level,
and response reliability. The average of the shadow curve thresholds
for 500, 1000 and 2000 cycles is 55 db. The lateralized SRT is 54 db
and agrees with the mean of the three puretone thresholds. The later-
alized PB score of 50% is what we expect from the method. The PB
score for the normal, contralateral ear is 98% and 2% less than per-
fect. We add the 2% to the obtained lateralized PB score. The PB
words were presented 15 db above the lateralized SRT as dictated by
the method. In this instance, the audiometric level was 54 + 15 or
69 db. The voice quality report was solicited at the 69 db level after
the PB score was obtained. The response, "sounds like you are in a
barrel 100 miles away," is normal. All four measurements are com-
patible with each other.

Name E.K. Age 39 Date 12-3-59

| 125 | 250 | 500 | 1000 | 2000 | 4000 | 8000 |

LATERALIZATION METHOD

1. Average FFA .... 58 db
2. Lat-SRT .... 55 db
3. Lat-FB .... 88 + 4%
4. Voice Report ...... Sounds pretty good.

5. Passed ____. Failed X .
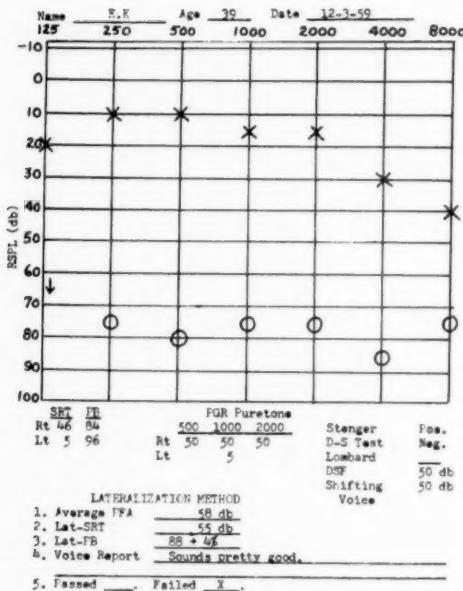
Fig. 3   Case 3

Figure 2 is the record of a male, aged 45, who failed the lateralization measures. The better ear (left) showed a 10 db threshold loss by speech audiometry, subjective puretone audiometry, and PGR audiometry. Speech discrimination was 98%. Patient claimed to have a deaf right ear. Puretone PGR audiometry revealed a 60 db organic hearing loss in the right ear. NR means no response.

CASE 2. The reader will note that the shadowgram does not have the proper shape. Also, the average of the three shadow curve thresholds (500, 1000 and 2000 cycles) is 67 db which is beyond the expected value (50 db ± 5). The level of the shadow curve should be about 50 db above the better ear since the skull attenuates the signal approximately 50 db for the three central frequencies. The lateralized SRT is 70 db (re audiometric zero) and is too high. It should be on the order of 60 db since the left ear showed a 10 db loss (10 db + 50). The explanation for the excessive PB score of 96% is that the PB words were perceived binaurally rather than monaurally. The average predicted PB score is 50%. The voice report, "sounds

very low, and seems near," may be indicative of binaural perception; however, this assumption may be questioned.

This patient failed three of the criteria of the lateralization method. There was a slight elevation in the puretone thresholds for the left or better ear. The over-all results suggest considerable residual hearing in the right ear rather than deafness.

The third illustration, Figure 3, concerns a male, aged 39, who claimed to have a deaf right ear. The evaluation began with the lateralization procedures.

CASE 3. The shadowgram does not parallel the puretone pattern of the better ear (left). The average loss for the shadow curve is 58 db which is slightly above the expected level. The lateralized SRT of 56 db is within the expected range. The PB score of 92% is about 42% too high and indicates binaural perception as does the voice quality report.

The audiological assessment was then completed and revealed the following: the speech thresholds were left 5 db, right 46 db; the PB score was 96% for the left ear and 84% for the right ear; the PGR thresholds were 5 db for the left ear and 50 db for the right ear.

As a point of interest, we will attempt to estimate the speech threshold for the right or poorer ear from the elevation of the lateralized PB score. The 5 db loss for the left ear plus 50 db for skull attenuation indicates that the lateralized SRT should be about 55 db as found. The reader will recall that the lateralized PB words are presented at a sensation level (SL) of 15 db, viz., lateralized SRT plus 15 db. In this case the audiometric level was 55 + 15 or 70 db. Since the lateralized PB score was 92% we can interpolate the sensation level in an approximate manner. We may ask what SL will give a 92% PB score in the normal, ipsilateral ear. From Hudgins, *et al.* (1947), we follow the increase in PB intelligibility as a function of sensation level. The estimated level which will yield a 92% score is about 30 db. In other words, if the PB words are presented monaurally to a normal ear at a SL of 30 db, we would expect, on the average, a score in the neighborhood of 84 to 94% for a normal ear.

Since the PB score was elevated 42%, we can arbitrarily convert this score into db from the Hudgins data. The 30 db SL referred to in the above paragraph is 15 db higher than the level specified by the Lateralization Method. This would indicate that the patient was per-
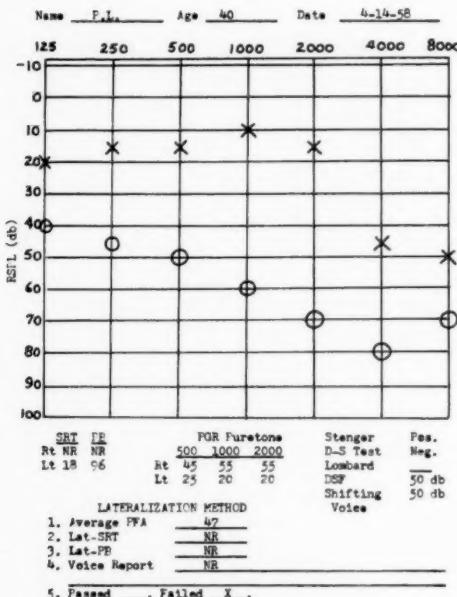
Fig. 4   Case 4

ceiving the PB words at a SL of 30 db in the left ear instead of 15 db. Now we can, attempt to estimate the organic speech threshold in the *right* ear.   Let us return to the audiometric level at which the PB words were presented.   This level was 70 db.   From this we subtract 50 db for skull attenuation and add the loss for the better ear (5 db) plus the 30 db extrapolated SL.   To wit, $70 - 50 + 5 + 30 = 55$ db.   The PGR thresholds were 50 db and the SRT was 46 db for the poorer ear indicating at least relative agreement between our extrapolation technique and the organic speech threshold in the right ear. This formula works if the Lat-SRT is correct.   This technique has not yet been validated.

Occasionally, we find that the Lateralization Method reveals unusual psychophysical responses.   We have selected one of these cases and his data are summarized in Figure 4.   This patient, aged 40, would not give any responses to speech audiometry in the right ear, either during subjective speech audiometry or during the Lat-SRT procedure.   He shows a functional overlay in the right ear.

Name ___E.C.___ . Age ___48___ . Date ___10-19-59___

| | 125 | 250 | 500 | 1000 | 2000 | 4000 | 8000 |

<table>
<tr><td colspan="2">SRT</td><td>PB</td><td colspan="3">PGR Puretone</td><td>Stenger</td><td>Pos.</td></tr>
<tr><td>Rt</td><td>50/30</td><td>9P</td><td>500</td><td>1000</td><td>2000</td><td>D-S Test</td><td>Neg.</td></tr>
<tr><td>Lt</td><td>0</td><td>92</td><td>Rt 20</td><td>20</td><td>25</td><td>Lombard</td><td>___</td></tr>
<tr><td></td><td></td><td></td><td>Lt</td><td>0</td><td></td><td>DSF</td><td>25 db</td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td>Shifting</td><td>20 db</td></tr>
</table>

LATERALIZATION METHOD   Voice

1. Average PFA _____ 48 db
2. Lat-SRT _____ 20 db
3. Lat-PB _____ 16 %
4. Voice Report ____ I can hear you talking but can't
   make out the words. I can barely detect your voice.
5. Passed _____ . Failed __X__ .
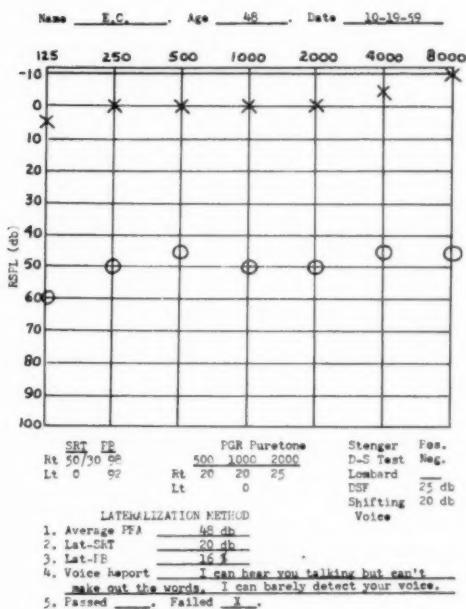
Fig. 5   Case 5

CASE 4.   The speech threshold was 18 db for the left ear with
a discrimination score of 96%.   The Stenger test was positive.   De-
layed Speech Feedback, PGR puretone audiometry and the Shifting
Voice test supported an organic hearing loss of 50 db for the right
ear.   The Doerfler-Stewart test was negative.   The PGR responses
supported the puretone loss and the 18 db speech threshold for the
left or better ear.

This patient failed the Lateralization Method on all four of its
criteria.   The shape of the shadowgram is incorrect for a deaf ear
in the presence of a verified 18 db loss in the better ear.   We know,
of course, that there is about a 50 db loss in the poorer ear as shown
by the other audiological tests.   The patient would not give a Later-
alized SRT, Lateralized PB score or any response to the voice quality
report.   He failed to respond even when the audiometric level of
the speech stimuli was 100 db delivered to his "deaf" ear.   We are

reasonably certain that his better ear was being stimulated by the stimuli in the Lateralization procedures.

Our fifth patient, aged 48, failed the Lateralization Method despite the fact that he shows a normal left ear and has a 20 db organic loss in his right (Fig. 5). We have the impression that he was voluntarily unco-operative regarding the status of his right or poorer ear during the determination of the shadowgram and the Lat-PB score.

CASE 5. The functional hearing tests (PGR puretone, the Stenger, Delayed Speech Feedback and the Shifting Voice test) support a 20 db loss in the right ear. By subjective or conventional speech audiometry he dropped from a 50 db speech threshold to a 20 db level after repeated measurements. His speech threshold for the left ear was normal. Speech discrimination was 98% for the right ear and 92% for the left ear.

From the lateralization criteria, his shadowgram is normal for shape only. The *level* of the shadow curve thresholds is approximately 30 db too high since we know that his loss in this ear is no greater than 20 db as verified by the other tests. Curiously enough, the first speech threshold obtained for the right ear was 50 db which corresponds to the level of his shadowgram. His "lateralized" SRT is 20 db which gives reliability to the subjective SRT for this ear. The "lateralized" PB score is 18% which is too low in view of the 98% he gave during standard speech audiometry. (The PB words are presented at a SL of 40 db during standard speech audiometry.) The voice report, "I can hear you talking but can't make out the words. I can barely detect your voice," may be indicative of binaural speech perception and poor co-operation. In this example, the patient was receiving the PB words in his right ear 35 db above audiometric zero and at a sensation level of 15 db. His PB score should have been on the order of 50% according to the Hudgins data. When the monaural loss is 50 db or less, the PB loss in the better ear should *not* be added to the Lat-PB score since the stimulus is not lateralized.

SUMMARY

The present report is a follow-up discussion of a set of procedures for verifying monaural deafness referred to as the Lateralization Method. The method involves four separate measurements which utilize subjective, puretone, air conduction audiometry and standard speech audiometry *without masking*. The procedures are applicable to monaural hearing loss cases where the loss in the better ear does

not exceed 50 db and where the poorer ear shows a loss ranging from 50 db to total deafness. The method is to be used along with the other functional hearing tests (PGR, Stenger, Lombard, Delayed Speech Feedback, etc.).

The results of the Lateralization Method offer valuable information about the presence of monaural deafness, the extent of the monaural non-organic hearing loss, if present, and the response integrity of the patient. Five illustrative cases were discussed to demonstrate the interpretation of the method. The present report stems from 60 adult cases of monaural deafness who were referred to our clinic for an audiological assessment. The method may be applied in approximately twenty minutes by the experienced clinician. The author is accumulating data for a third report which will enlarge the scope of the application and interpretation of the method.

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A STUDY OF PGSR TESTING
OF RH ATHETOIDS

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A group of 30 athetoids with known hearing impairment and an etiology of erythroblastosis were tested by PGSR, pure tone, and speech audiometry.

Erythroblastosis is known by various names as erythroblastosis fetalis, jaundice, hemolytic disease, icterus neonatorum, kernicterus and others, the pathology results in one case among twenty Rh negative blood factor females who mate with an Rh positive male. Erythroblastosis is present in one out of every 300 births.

The Rh factor is a blood agglutinogen which naturally occurs in the red blood cells of approximately 85 per cent of white persons. The genetic composition of the parents determines whether the red cells have (Rh positive), or lack (Rh negative), this factor.

During the first pregnancy resulting from the union of Rh positive males and Rh negative females, the mother develops antibodies against the foreign agglutinogen of her own child in utero. In the second or any subsequent pregnancy of the woman sensitized by a previous Rh positive pregnancy the antibodies in the mother's blood pass over into the circulation of the fetus and here cause destruction of the fetal Rh positive blood. This process in the fetus resulting from Rh factor incompatibility is the erythroblastosis of this study.

If the reader desires further reading into the Rh factor, he is referred to the words of Landsteiner and Wiener,[1] Levine,[2] Potter,[3] Lande,[4] Docter,[5] Diamond,[6] Sturgeon,[7] and Goodhill.[8]

Phelps classified the term Rh athetoid based on 1) athetosis; 2) inability to move the eyes up and down, but with perfectly good

control laterally; 3) a hearing loss; and 4) all having Rh factor difficulty or erythroblastosis.

The experimental subjects were 30 Rh athetoids ranging from seven to fourteen years of age with a mean of 11.4 years. Selection of subjects was based on pediatric, otologic, and neurologic examinations, blood studies and demonstrable hearing loss. The subjects were chosen from case histories, medical records, Rh blood studies, and individual interviews.

Variable factors were taken into account, and controlled as much as possible. Each child selected had an electro-encephalographic test and psychometric workup. These were equated along with schooling. These children were also seen by the experimenter for training over a two-year span which facilitated rapport, so necessary for hearing testing of young children.

The PGSR instrumentation employed is similar to that developed by Richter in the Phipps Psychobiologic Laboratory and elaborated on by Hardy and Bordley at the Johns Hopkins University School of Medicine. The basic equipment consists of the following units:

1. An experimental Maico psychometer, Model WD-10084. The Maico electrodes and shocking device were not used. Other described components were used.

2. A shocking apparatus utilizing a condenser discharge circuit.

3. Two pairs of polished zinc electrodes, thin, about ¾ inch diameter, with 12-foot leads.

4. A paste made of kaolin in a saturated solution of zinc sulfate.

5. A 2-inch wide rubber band and adhesive tape for fastening the electrodes in place.

6. An ADC audiometer with binaural headphones.

7. A Wallace and Tiernan, model F-194, 0-5 milliampere D.C. ink recorder, with recording graph. A circular recording type graph was used, which made it easier to read the entire record and facilitated the length of recording possible.

TABLE I

MEANS OF FREQUENCY, EAR, AND METHODS OF TESTING
THRESHOLD ACUITY INTERACTION FOR
THE RH ATHETOID

FREQUENCY	PGSR		PURE TONE	
	Right	Left	Right	Left
512	18.42	17.46	23.21	18.41
1024	20.31	19.31	30.64	22.64
2048	47.86	32.40	52.57	40.31
4096	42.41	32.61	56.41	42.29

PROCEDURE

PGSR testing was administered first, because it was felt that this would be a more objective procedure of first getting a GSR graph and then matching it with pure tone and speech reception tests. All testing was done at the examiner's office in a sound-treated and control room in the audiological suite.

Since rapport had previously been established, and these children were in a higher age range, no toys were introduced and distractions were kept at a minimum. Each subject was briefly informed about the nature of the testing and reassured about the procedure, although no mention was made about the stimuli involved. To reduce the recording of muscle movement artefacts, each subject was informed of the effect on the record of any such movement and were instructed to relax and remain quiet. Co-operation was good and muscle movement was minimal. It was felt that the environment of the test situation was controlled, array of distracting stimuli reduced and the child's behavior stabilized so that responses significant of hearing were interpretable. A hearing response was characterized by two definite breaks on the graphic record with the deflection of the pen moving toward the periphery of the graph.

Within seven days of the completion of the PGSR test, the child returned to the office and pure tone and speech reception tests were run. The procedure for the pure tone audiometry was similar to the PGSR except now the child was instructed to raise his hand when a tone was heard.

Following this, the speech reception threshold was measured using spondee words presented through a visual medium. The equipment was calibrated and adjusted to yield an output comparable to the published records put out by Central Institute for the Deaf. The subject was shown a set of 36 pictures which were defined, each one representing a spondee word, and mounted on a large board. He was instructed to name or point to the picture of the word which would be heard over the headphones. The spondee words were read into the microphone with the emphasis carefully watched on the monitoring needle.

RESULTS

It is interesting to note that all thirty had bilateral hearing losses and all had a perceptive or mixed diagnosis for each ear. Only the four frequencies of 512, 1024, 2048 and 4096 cycles per second were tested. It was felt that these were the most important frequencies for speech reception and more reliable results could be obtained from a shorter testing period with this group. Galvanic skin responses could not be obtained on eight of this group so that PGSR-Pure Tone comparisons were only determined for the remaining 22.

From Table I, a hearing loss for the Rh athetoids at all frequencies tested and in both ears is observed.

Hearing was positively related to frequency, ranging in the right ear from a low of 23.21 db of loss at 512 cycles per second to a high of 56.41 db of loss at 4096 cycles per second for the pure tone air conduction data. In the left ear, a similar relationship is seen, with a low of 18.41 db at 512 cycles to a high loss of 42.29 db at 4096. The left ear data was 5 to 10 db below the right. PGSR results showed .95 db to 14 db better acuity than pure tone data along the testing range.

The employment of the PGSR audiometric technique in the Rh athetoid showed interesting deviations from that seen in testing the hard of hearing without accompanying brain injury.[9] Latent periods were longer and more variable. More initial shocking was needed to set up conditioning, and skin resistance was continuously low. The base line drifted, and the peaks were sharper and of a shorter duration, with frequent short bursts of activity. The GSR could not be elicited for 26.6 per cent of this group.

All the subjects who were able to meet the demands of the pure tone test situation responded reliably to the spondee words, so that

speech thresholds for all 30 subjects were determined. The mean threshold for the right ear of this group was 38.63 decibels and 30.33 decibels for the left ear.

CONCLUSIONS

These results tend to confirm the hypothesis that erythroblastosis may damage portions of the inner ear or VIII nerve system in its gross destruction of the basal ganglia area which creates the athetosis. The possibility is brought out that the athetosis and the impairment of hearing acuity result from the same pathological process of erythroblastosis. Only further research will show if control of erythroblastosis will result in the elimination of the bilateral nerve type auditory impairment which is frequently seen in the athetoid.

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XIX

SARCOMA OF THE LARYNX

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AND

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Sarcoma of the larynx is a rare disease. Havens and Parkhill[16] reviewed the English literature for 30 years (up to 1939), finding 15 cases of sarcoma of the larynx. To this number they added 11 cases which were treated at the Mayo Clinic. The authors concluded that sarcoma occurred once to every 100 cases of carcinoma of the larynx.

Of the 45 additional cases we found in the literature, the incidence was twice as great in males as in females, metastases occurring in 8 per cent of the cases. Fibrosarcoma comprised 50 per cent of the reported cases; two cases of rhabdomyosarcoma were described.

In 1892, Bosworth[1] wrote: "The indications are for treatment with promise of success. The decision must be based on the size and location of the growth. The early lesion is best treated through the natural passages and if the endolaryngeal methods fail, one proceeds promptly with a thyrotomy. In aggravated cases, complete extirpation of the larynx is indicated." This may still be regarded as a classical description of the situation.

Because of insufficient follow-up and incomplete histologic data, we feel there is considerable uncertainty about the nature of many of the tumors described as sarcoma. This uncertainty is further increased by the work of Lane[19] who uses the term pseudosarcoma to indicate a presumably non-neoplastic connective tissue mass, histologically bizarre and deceivingly suggestive of some fully malignant form of true sarcoma capable of metastasis. As quoted by Lane,

Ewing mentioned "granulation tissue" sarcoma and traumatic myositis mistaken for sarcoma. The differential diagnosis between a mass-forming hyperplasia that does not threaten life and a true sarcoma may be exceedingly difficult. Lane describes 10 cases of upper digestive and respiratory tract lesions in which an anaplastic stroma of sarcomatous appearance (bulky and preponderant) may be associated with an inconspicuous and easily overlooked intramucosal or invasive squamous cell carcinoma. It was believed that only the carcinomatous portion had truly malignant neoplastic properties.

In the greater Cincinnati area, we are familiar with three cases of mesodermal tumor of the larynx. The incidence of this type of lesion is 0.5 per cent in our university hospital; at one of our private hospitals, 1 in every 36 cases of tumors of the larynx. A discussion of the three cases follows.

REPORT OF CASES

CASE 1. A 68 year old male, with dyspnea relieved by cough and aggravated in the supine position, was admitted to St. Elizabeth Hospital (Covington, Kentucky) on August 3, 1954. There were no palpable masses noted in the neck, nor any other abnormal physical findings. The patient was taken to the operating room on the day of admission and, utilizing 3 cc of 10 per cent cocaine and laryngeal spray, a 740-Jackson laryngoscope was inserted into the larynx, exposing a tumor attached to the right cord near the anterior commissure. The tumor had the appearance of a nasal polyp, but was firm, measuring two centimeters in diameter, grayish-white, smooth, and moving with respiration. The pedicle was grasped and the mass evulsed with a laryngeal biopsy instrument; no bleeding occurred. The patient was returned to his home the following day. At the time of this writing (six years later) there is no evidence of recurrence.

The tumor is a polypoid mass, measuring 2 x 1 x 1 cm. On one side is a stump, 5 by 3 mm. Sections reveal diffuse, grayish-white tissue and the mass to be generally devoid of epithelium; where present (presumptively at the base of the tumor) the epithlium is pseudo-stratified, columnar, and ciliated. Subepithelially, there is a focal moderately intense lymphocytic reaction, often periglandular. Clusters of mucous glands show slight dilatation. Throughout the lamina propria, which is fairly sharply delimited from the tumor, are fibroblastic activity, slight diffuse lymphocytic infiltration, and a clump of several voluntary muscle fibers.

TABLE I

SUMMARY OF CASES FOUND IN THE LITERATURE

REF. NO.	AGE	SEX	DIAGNOSIS	RESULT	METAS.	MICSCP. DESCRP.
2	66	M	Fibromyxosarcoma	Cured 4 yr.	?	No
3	58	M	Fibrosarcoma	Cured 5 ½ yr. Died C.V.A.	No	No
3	75	M	Plasmacytoma	Cured 13 mo. Died C.V.A.	No	Yes
3	49	M	Lymphosarcoma	Cured 12 yr.	No	Yes
3	51	M	Fibroangio-osteosarcoma	Recur. Died	Yes	No
3	55	M	Fibrosarcoma	Cured 4 ½ yr. Cardiac death	No	No
3	58	M	Fibrosarcoma	Cured 5 yr.	No	No
3	25	M	Fibrosarcoma	Cured 1 yr., no recur.	No	No
3	55	M	Chondrosarcoma	Cured 1 yr., no recur.	No	No
4	76	M	Fibrosarcoma	?	?	No
5	47	M	Fibrosarcoma	No recur. 6 mo.	No	Yes
5	?	?	Neurogenic sarcoma	No recur., died 2 yr.	No	No
6	62	F	Fibrosarcoma	No recur. 3 mo.	No	No
6	59	?	Undetermined	No recur. 1 mo.	No	No
7	68	M	Fibrosarcoma	Died 8 ½ mo.	Lung,Neck	Yes
8	69	M	Fibrosarcoma	Cured 5 yr.	No	Yes
8	65	M	Fibrosarcoma	Cured 1 yr. 3 mo.	No	No
9	61	F	Fibrosarcoma	Died 16 mo.	No	No
9	69	M	Fibrosarcoma	Cured 8 yr.	No	No
9	73	M	Fibrochondrosarcoma	Cured 3 yr. 7mo.	No	No
9	71	M	Fibrosarcoma	Cured 6 mo.	No	No
10	62	M	Hemangio-endothelioma	Cured 9 mo.	No	No
10	40	M	Hemangio-endothelioma	Cured 15 mo.	No	No
10	43	M	Fibrosarcoma	Cured 3 ½ yr.	No	No
11	31	M	Fibrosarcoma	Cured 6 mo.	No	Yes
12	28	F	Leiomyosarcoma	Cured 1 ½ yr.	No	Yes
13	10	M	Rhabdomyosarcoma	Cured 4 yr.	No	Yes
14	58	M	Fibrosarcoma	Cured 8 mo.	No	Brief
15	50	F	Fibrosarcoma	?	?	?
17	24	M	Fibrosarcoma	Recur., died, ? time	Yes	No
18	52	M	Fibrosarcoma	No recur. 6 yr.	No	Yes
18	63	F	Lymphosarcoma	Pulm. Throm., 9th day	No	No
20	40	F	Chondrosarcoma	No follow-up	?	Yes
21	45	M	Lymphosarcoma	Cured 10 yr.	No	No
22	51	M	Fibromyxosarcoma	? Cured	No	No
22	56	F	Chondrosarcoma	? Cured	No	No
23	23	F	Lipomyxochondroma	Cured 1 yr.	?	Yes
24	17 days	M	Fibrosarcoma	Died 115 days	No	Yes
25	62	M	Chondrosarcoma	No recur. 4 mo.	No	Yes
26	68	F	Rhabdomyosarcoma	Cured 6 mo.	No	Yes
30	14 wks.	M	Hemangio-endothelioma	Died 22 hr.	No	Yes
31	?	F	Hemangiosarcoma	Died. ? Time	Neck	No
32	?	?	?	Cured 2 yr.	No	No
34	65	M	Angiosarcoma	Cured	No	No

The tumor mass consists of a collagenous matrix with a fairly uniform distribution of generally discrete, large cells throughout. Centrally, collagen predominates; peripherally, the tumor is cellular with some tendency to arrangement into poorly delimited clusters and bundles. Scanty, compressed capillaries show no particular patterning. There is considerable variation in cell size and shape; however, several types can be delineated.

The predominant cells are large, ovoid and have poorly delimited granular cytoplasm. The nuclei comprise approximately two-thirds or more of the cells, and are generally vesicular with scattered fine and coarse chromatin. Some nuclei have prominent nucleoli. Additionally, there is a moderate number of hyperchromatic irregular nuclei. These cells are characterized by fibrillar or granular cytoplasm. Occasionally, such cells are coarsely stellate. While tadpole cells are less frequently seen, mitotic figures are fairly numerous. Throughout, but chiefly in the peripheral portions, there are irregular giant cells. These are generally round or ovoid and have vacuolated, centrally pale cytoplasm. The nuclei possess coarse chromatin and prominent nuceoli. Other giant cells are characterized by broad fibrillar cytoplasmic masses; some cut longitudinally appear straplike. Giant tadpole cells are also noted. Cross striations are not noted within the cytoplasm of these large cells, nor are they seen after careful and long search of slides stained by the P.T.A.H. or Bodian methods (Fig. 1).

Trichrome stain reveals these cells to be generally characterized by a bright acidophilic fibrillar cytoplasm. Foot and Foot reticulin stain reveals delicate and coarse reticulin fibers in close relation to each cell. When the cells are arranged in whorling bundles, the reticulin fibers are of longitudinal or whorled pattern. Nerve fibers are not demonstrable. Schiff stain is negative; phosphomolybdic acid stain for lipids is positive. Fat stains were not done.

The original impression was that of rhabdomyosarcoma. Consultation with local pathologists was in part confirmatory, some considering it to be a sarcoma of unclassifiable type. Consultation with the Armed Forces Institute of Pathology resulted in a divergence of opinion, liposarcoma, rhabdomyosarcoma, low grade sarcoma of undetermined type, and bizarre fibroma being suggested.

CASE 2. An 81 year old negro was first seen in the emergency room of the Cincinnati General Hospital on September 24, 1952. He was comatose when examined by the otolaryngology resident. He
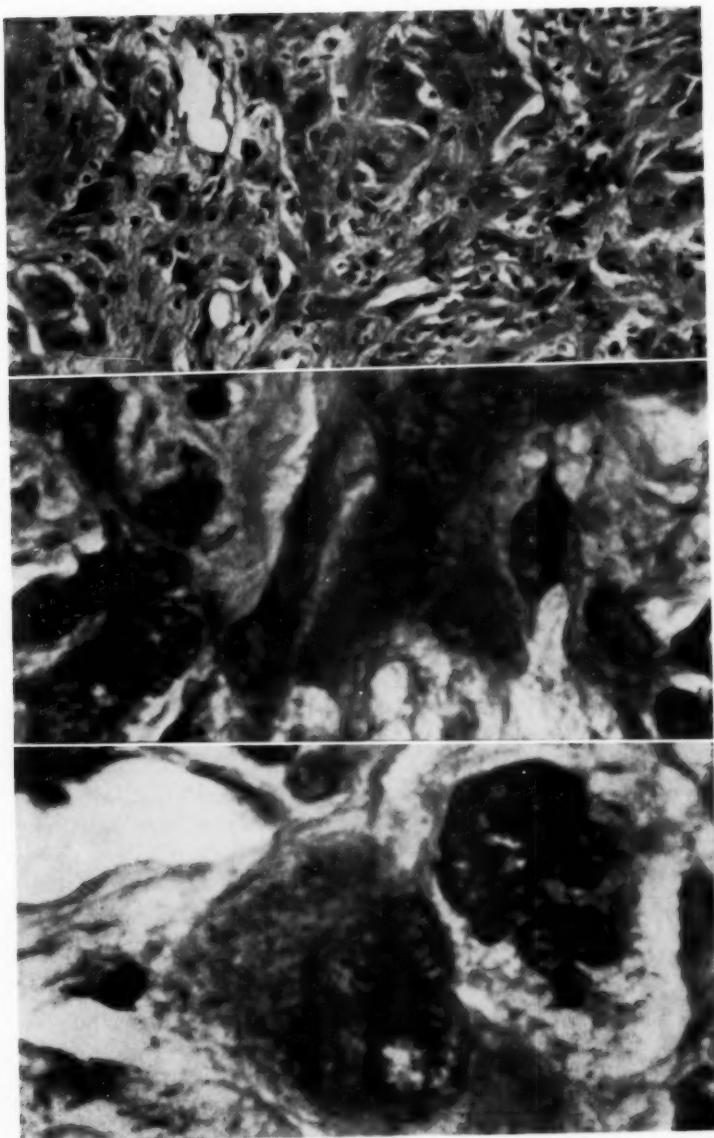
Fig. 1.—Photomicrographs of tissues from Case 1.

was subsequently admitted with a diagnosis of status asthmaticus. Direct laryngoscopy showed a large, irregular, marble-sized "ball valve" tumor attached anteriorly to the left vocal cord. Tracheotomy gave immediate relief. A suspension laryngoscopy was done one week later and the tumor was removed in four pieces. Pathologic diagnosis: fibrosarcoma.

About six months later, the patient was admitted to a chronic disease hospital with recurrent sarcoma of the larynx. Emergency tracheotomy again was done, followed by an x-ray diagnosis of metastatic lesion in the right lower lung field. Palliative x-ray therapy to the larynx was given and the tracheotomy tube was subsequently removed. On February 25, 1954, recurrence of a polypoid tumor above the anterior commissure was noted. The cords were not involved; there was little change in the metastatic lesion in the lung. Apparently, the cervical lymph nodes were never involved. The tracheotomy tube was reinserted on July 15, 1954. Four months later the patient was found dead in bed. No autopsy was done.

Tissue specimens varied in size from 5 to 15 by 10 millimeters in greatest dimension. The surface of all portions is characterized by small and broad, sessile, polypoid, flat irregularities. The mucosa, for the most part, is absent; where present, is seen as short strips or clumps. The epithelial clusters rarely present disturbance in stratification, rare dyskeratotic cells with enlarged irregular nuclei. There are small, irregular, persistent strands of epithelium in relation to the clefts at the sides of polypoid structures. Throughout, the epithelium is sharply delimited from the underlying cellular stroma.

Basically, the tumor presents a loose collagenous stroma, more compact centrally and basally. There is fairly uniform cellularity, somewhat more so in the periphery. Cells are arranged along courses of collagen fibers into streaming, whorling bundles which are cut in various planes. Small, poorly formed vortices are noted throughout.

Irregularly ectatic capillaries pass throughout the cellular stroma, fairly evenly and widely spaced. Superficially, many of the polypoid masses present broad bands of superficial necrosis with a polymorphonuclear cellular infiltration. Capillaries throughout this region often present fibrinoid walls and thrombosis. The stroma of the polypoid masses is characterized by generally large cells of varying shapes with fibrillar eosinophilic cytoplasm. The predominant type of cell is bipolar with lesser numbers being unipolar or multipolar. Nuclei are

generally vesicular with single or double nucleoli. Scanty numbers of cells have irregular compact, hyperchromatic nuclei. Moderate numbers of giant cells with similar vesicular, less often hyperchromatic nuclei, are noted. There are occasional mitotic figures. Cross striations are not seen.

CASE 3. A 48 year old male was admitted to Good Samaritan Hospital (Cincinnati, Ohio) on August 1, 1950, with a chief complaint of hoarseness. Direct laryngoscopic examination showed a smooth, polypoid, grape-sized tumor attached to the left vocal cord. Seventeen days following biopsy, the tumor was removed through a suspension scope. The diagnosis was fibrosarcoma.

Three-year follow-up examination revealed no evidence of recurrence of tumor in the larynx or throat. Shortly thereafter the patient developed tuberculous meningitis and was hospitalized for three months. He was treated with streptomycin and isoniazid, recovering completely. The patient again was seen in March, 1956, at which time an x-ray of the chest showed a left upper lobe mass. There were no mediastinal nodes. The mass proved to be bronchogenic carcinoma. A left pneumonectomy was done and the patient made an uneventful recovery. About three months later he was hospitalized because of chills and fever, and died on the fifth hospital day. There was no evidence of cancer at autopsy. Death was due to coronary thrombosis.

There are two portions of laryngeal tissue. One measures 5 by 3 millimeters; the other, 7 by 5 millimeters. The changes observed in both epithelium and stroma are similar in all sections.

The mucosa covers two-thirds to three-fourths of the surface of a nodule and is deficient along one margin, presumptively representing the base. Generally of normal thickness, the mucosa presents foci of thinning. Superficially there is increased cornification; rarely, small clusters of granular cells. The middle two-thirds of the epithelium is composed of large polygonal cells with slightly accentuated spinous processes. An occasional polygonal cell presents single or multiple, large or small, keratin granules and pyknotic nuclei. Focally, the mucosa presents a plaque of thickening. There are numerous cells characterized by vesicular distention and disruption of cytoplasm within the region of thickening. Here, also, some distortion of cellular stratification and smudging of cell borders is present. Inclusion bodies are not seen. Generally, the basal layer of the epithelium is composed of regularly oriented and sharply delimited cuboidal cells.

There are occasional clefts at the stromatomucosal junction with the basal layer. The basal epithelium, in relation to such clefts, is often partially filled with blood, proteinaceous material, or both; presenting some reduplication with loss of cellular orientation and slight cellular enlargement. Rarely, in relation to these basal cell layer changes, is there loss of the sharp demarcation between epithelial and stromal cells.

The stroma consists of loosely arranged, generally coarse, hyalinized collagen with some suggestion of eddy formation. Diverse types of cells lie haphazardly in the interstices. The central and basal portions are less well populated than the peripheral one-third. Here, cells predominate and focally impinge upon the basal layer of the epithelium, or are sloughed into junction vesicles located at the dermato-epidermal border.

Within the outer third, the principle cells are giant size and bizarre. Nuclei are large, lobulated, hyperchromatic, and often have single or multiple prominent nucleoli. Mitotic figures, some of which are multiple, are fairly frequent. Cytoplasm is moderate in amount. Many cells are irregularly ovoid; others have multiple processes, and some present long, coarse, terminal cytoplasmic extension. In addition, there are band forms with syncytical nuclear masses. Although the cytoplasm is acidophilic and granular, fibrils are only suggested and cross striations are not to be demonstrated.

More centrally, the predominant cell is considerably smaller, irregularly ovoid or elliptical, and often characterized by bipolar or multipolar cytoplasmic coarse processes. Their nuclei are generally similar to those of the giant cells seen more peripherally.

Two small foci of isolated epithelium are found within the stroma, one 300 micra from the basal layer and the other approximately 1 millimeter from the basal layer. These cells are adult in appearance, characterized by spinous processes, regularly arranged, and are regarded as epithelial inclusions.

COMMENT

The photomicrographs of Case 1 are representative also of the findings in Cases 2 and 3.

There are associated laryngeal mucosa and dyskeratotic changes of the mucosa in two of the three cases. In one of the two cases there

are sparse, small, isolated nests of squamous epithelium which are regarded as sequestered epithelial inclusions.

Granular cytoplasm, frequent mitotic figures, and bizarre giant cells with single and multiple nuclei are exceedingly uncommon in fibrosarcoma.[27] If such cells appear in considerable numbers, the tumor generally proves to be either liposarcoma, rhabdomyosarcoma, or leiomyosarcoma—rather than fibrosarcoma.

Poorly differentiated myxoid liposarcoma is characterized by monstrous giant cells with variable nuclear configurations. Little fat is produced in this type of liposarcoma; however, cells with pyknotic nuclei and vacuolated cytoplasm should be demonstrable. Criteria for the diagnosis of rhabdomyosarcoma, as enumerated by Wolback,[33] Stout[28] and others, are in part fulfilled by the conditions seen in these cases. It is important to emphasize that cross or longitudinal striations (singly or together) while convincing, are not mandatory for the identification of rhabdomyosarcoma. Frequently, cross striations are presented imperfectly if at all.

Despite the histologic resemblance of the three cited cases to mesodermal sarcoma, they are also similar to peculiar mesodermal reactive tumors which have been described in subcutaneous tissue. These tumors are designated by a variety of names, the most common being pseudosarcoma.

Other observers have commented upon the lack of correlation between the clinical outcome and the histologic appearance in cases of so-called sarcoma of the larynx. Of the 45 cases reviewed for our report, only six had a five-year follow-up. The data published, for the most part, does not permit a conclusion as to the potentialities of the lesion.

In Case 1 the patient showed no evidence of recurrence after six years. As reported in Case 2, the patient developed recurrence of a polypoid tumor six months after fractional removal. At this time, an x-ray density was seen in the lung; further attempt at removal of the laryngeal lesion was not made. The patient expired following palliative x-ray therapy. No autopsy was done. In Case 3, bronchogenic carcinoma was noted five years after excision of the laryngeal lesion, for which a left pneumonectomy was done. Shortly after removal of the lung, the patient died of coronary thrombosis. Autopsy observation showed no evidence of laryngeal or lung malignancy.

Thus, in two of the three reported cases, there was no evidence of recurrence despite simple removal of the lesion and no other therapy. In view of the natural history of these cases and the similarity to subcutaneous pseudosarcoma, the original diagnosis of sarcoma of the larynx does not appear to be substantiated.

SUMMARY

Three cases of mesodermal laryngeal tumors are presented which are thought to represent pseudosarcoma.

It is our opinion that, until more is known, masses presenting a sarcomatous appearance should be classified as pseudosarcoma and treated conservatively, much as described by Bosworth in 1892.

The subject of sarcoma of the larynx needs further study. After thorough review of the literature, the authors find it difficult to establish conclusive diagnosis, treatment, and prognosis of this type of lesion.

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XX

POSITIONAL VERTIGO AFTER
STAPEDECTOMY

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The principal purpose of this report is to help clarify the etiology of peripheral positional nystagmus and vertigo. A secondary purpose is to report vestibular reactions after fenestration of the oval window.

Routine observation has indicated that many patients exhibited spontaneous nystagmus after stapedectomy. The duration varied from minutes to days; the intensity from first degree to third degree. The fast component of the nystagmus was sometimes directed to the side of the operation, sometimes to the opposite side. The intensity and duration of this spontaneous nystagmus seemed proportional to the trauma to the vestibule sustained at operation. Clinically, the types of trauma that caused most harm were pressure into the vestibule and suction. Blood in the vestibule and burring over the footplate did not instigate vertigo as much as did mechanical manipulations.

I have routinely examined stapedectomy cases for positional nystagmus and vertigo about a week after operation. I have not observed positional nystagmus except in the cases reported here. The cochlear aspects will be reported only briefly, as the emphasis here is on the vestibular aspects. Each patient had otosclerosis. In the first two patients, positional vertigo was ascribed to a large piece of the footplate lost in the vestibule.

REPORT OF CASES

CASE 1. J.K., male, aged 49, underwent a right stapedectomy, Shea type, on November 6, 1959, for otosclerosis. A vein graft was inserted and a four millimeter polyethylene strut was used. At operation, the footplate broke around the periphery and almost the entire footplate bobbed around in the vestibule like a cork. Cautious attempts at removal failed. From the experience of others, I had learned

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From the Vertigo Clinic, Temple University Medical Center.

that the trauma of removing such a piece could ruin cochlear function so the piece was permitted to remain and was covered with a vein graft. On November 16, positional tests for nystagmus and vertigo elicited no reaction in the left supine position but, in the supine position with head hanging, there was a rotatory nystagmus to the right and vertigo. In the supine position with head turned to the right, there was a violent rotatory nystagmus to the right plus vertigo. On sitting up after each of these positions, there was nystagmus to the right. Follow-up examination on December 12, 1959, March 19, 1960, and May 21, 1960, revealed rotatory nystagmus to the right with pronounced vertigo in both the supine position and in the right lateral position. At re-examination on September 23, 1960, the patient reported that the dizziness had disappeared about July. No positional nystagmus and vertigo could be elicited. He was able to work on ladders and at heights. He added that he had sustained a concussion on September 1, 1960, but this had in no way affected his ear. Incidentally, he had achieved and maintained an excellent hearing result with speech reception threshold at the 5 decibel line and a discrimination of 96%.

CASE 2. O.D., female, aged 69, underwent fenestration of the right oval window on August 19, 1960, with insertion of a vein graft and a 3.5 millimeter polyethylene strut. The footplate broke around the periphery in one piece and it was decided to let it remain. On August 25, there was no spontaneous nystagmus but there was positional nystagmus in the supine position with head hanging and in the right lateral position. The result was more violent in the right lateral position, with rotatory nystagmus to the right and vertigo. On September 20, examination showed positional nystagmus and vertigo in the supine position with head hanging but not in the right lateral position. She also achieved a good hearing result.

In the following case, the positional vertigo and nystagmus were ascribed to an extra long polyethylene prosthesis. At that time, we had thought that the hearing might be improved with a longer prosthesis, giving more pressure into the vestibule.

CASE 3. A.U., female, aged 53. This patient had a unilateral otosclerosis. On February 15, 1960, a fenestration of the left oval window was performed, with removal of the sclerotic footplate. Here, a vein graft was not used but gelfoam was placed and a five millimeter strut was fitted onto the lenticular process of the incus. In fitting it onto the incus, the strut was pushed rather deeply into the vestibule. (Subsequently, I adopted the two-handed technique of House, of

raising the incus with a hook while fitting the strut onto the lenticular process with a strut guide.) This maneuver precipitated vertigo and vomiting on the table. The patient developed third degree nystagmus to the other side. However, she went on to achieve a speech reception threshold of between 5 and 10, and a discrimination test of 94%. Tests for positional nystagmus and vertigo on March 16 and again on April 13, 1960, disclosed a rotatory nystagmus to the right in the supine position but nothing in the side positions. On April 13, the supine position caused a left rotatory nystagmus and vertigo but the side positions elicited no response. There was no spontaneous nystagmus. She has not been examined since then.

The following case of positional vertigo is most probably due to head trauma independent of the fenestration of the oval window.

CASE 4. E.J., male, aged 34, had undergone a left stapes mobilization in September, 1955, but this was unsuccessful. In September, 1959, I performed a Shea operation. This was successful and he discarded his hearing aid. In March, 1960, a Shea operation on the right also obtained a good result. On August 7, 1960, in an auto accident he sustained a severe concussion, and required hospitalization elsewhere for two weeks. On August 24, my examination disclosed rotatory nystagmus to the left in the right lateral position. His hearing was not impaired by the accident. He complained of a sensation of fluid in the left ear but paracentesis produced none. Since then, the positional nystagmus and vertigo have continued, although less severely.

These cases fulfilled Cawthorne's[1] criteria for positional nystagmus of benign peripheral origin. Latency, duration and direction corresponded to his description. However, the nystagmus was not typically fatiguable and the vertigo on the second and third tests was almost as tumultuous as on the first test.

Lindsay and Hemenway[2] reported a case in which autopsy revealed a mass of vessels pressing on Scarpa's ganglion with marked degeneration of the nerves to the utricle and the superior and horizontal semicircular canals. They ascribed postural vertigo to unilateral sudden partial loss of vestibular function. My cases fitted this pathologic classification. In contrast, I observed a case in which complete cochlear deafness followed a stapedectomy. In this case no positional nystagmus or vertigo could be elicited, either subjectively or objectively at any time.

Adolph Meihlke[3] was able to produce, in rabbits, positional nystagmus and vertigo by placing a drop of human blood in the

perilymph space of the pars superior of the labyrinth.   He ascribed this to compression.

CONCLUSION

Cases of positional nystagmus and vertigo are reported in which pressure in the perilymphatic part of the vestibule appeared as the causative factor.

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XXI

THE EFFECTS OF IONIZING RADIATION ON THE EAR

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Teleradiation from Cobalt 60, high voltage x-ray and radioactive sources for malignant head and neck tumors often involve the region of the end organs of the hearing apparatus. The question arises, how the rather high tumor doses affect the delicate structures of the cochlea, the middle ear and the ear canal and whether they cause any deficit (temporary or permanent) in the function of this end organ.

The effects of conventional x-ray on the ears of experimental animals has been studied by several writers but the data concerning the effects of gamma radiation on the function of hearing of human subjects and on the pathologic changes in the region of the ear are rather meager.

Kelemen[1] exposed pregnant albino rats to x-ray at midterm and examined their litter histologically close to term. He found the auditory and vestibular end organ structures intact, amid extensive hemorrhage in their vicinity and against a background of severe radiation induced endocranial deformities.

Novotny[2] exposed guinea pigs to x-ray radiation, using doses as high as those commonly used in cancer therapy. He found a slight, but clearly observable deterioration of the hearing function of the test animals. The decrease has been measured by the Wever and Bray effect. The average hearing loss found was 8.4 decibels and was localized in the 4000 cps frequency range. Microscopic examination of the cells of the cochlea did not show detectable changes from normal structures. The intralabyrinthine pressure was also unaltered.

He considers the microscopical changes reported by previous authors as artifacts.

There was considerable interest in some early reports of the possible benefits of x-ray irradiation on various pathologic conditions of the ear associated with hearing deficit, but most of these reports were inadequately supported by scientific evidence. The irradiation therapy for hearing loss of various etiologies have been abandoned except for radiation of lymphoid elements in the auditory tube or nasopharynx because the result was unpredictable.

Girden[3] studied the effects of x-ray radiation in dogs and reported a transient gain in acuity of about 5.5 db, lasting from two to five weeks which was then followed by a relapse to the previous level of acuity. He felt that the gain in acuity cannot be attributed directly to the ionizing effect produced by roentgen rays since atoms are ionized by x-radiation for only 10^{-9} seconds. A study of the auditory action currents and the cochlear effect, before and after irradiation, corroborates the functional findings, i.e., there were not any noticeable changes produced immediately after irradiation. He cannot give an explanation for the transient improved hearing.

X-irradiation for otosclerosis has also been tried, but long abandoned because of the inconclusive results.[4] Irradiation of otosclerotic foci with high energy particles such as a proton beam has been used in animal experiments by Nylen, et al.[5] The proton beam is directed extracranially against the otosclerotic foci in the labyrinth, while beta-emitters are introduced through the eustachian tube or placed directly in the middle ear following tympanotomy. The beta-particles and protons destroy the organic compounds of the otosclerotic foci, while the inorganic compounds are removed by chelating agents.

SUBJECTS AND METHODS

Fourteen subjects ranging in age from 12 to 70 were treated at University Hospital, Baltimore, Maryland, by the Radiotherapy Department with a Theratron Junior Cobalt Teletherapy Unit for head and neck tumors, and then followed up and investigated at the Otolaryngology Division. Ten subjects had carcinoma of the nasopharynx, two had carcinoma of the maxillary sinus with orbital involvement, one had pinealoma and one had ependymoma. These patients received between 4000 and 6000 r radiation at the region of the cochlea. Each patient used as a subject in the investigation was given a pure tone air conduction and bone conduction test on a Beltone

15-A calibrated audiometer by the same trained tester in a sound treated IAC (Industrial Acoustic Company) 402 CT Audiometric Testing Room before the initial and after the final period of radiation. Additional tests were given at intervals during the various stages of treatment. The findings of the pure tone tests were corroborated by speech reception threshold tests. In addition, special interest was focused on the presence and degree of recruitment which might exist at any stage of the investigation of the patient's hearing. The recruitment phenomenon was tested by means of the "Region of Comfortable Loudness" test[6] and, where practicable, by means of the "Loudness Balance" test (binaural and monaural).[7] Each patient was asked to describe changes in this hearing as to the presence or absence of tinnitus.

Due to the relatively small number of cases studied, it did not appear justified to submit the results to statistical analysis, but rather indicate what is characteristic of this special group of patients.

RESULTS

From comparison of the test results obtained in this study on patients treated with CO 60 in the region of the hearing mechanism, we observed that the cobalt radiation affected individuals selectively. Changes in hearing threshold acuity occur in some patients and not in others. Where hearing threshold shifts do occur, the shift is not great.

Initially, there were two subjects with normal hearing, nine with perceptive and three with conductive hearing losses. On the basis of the number of ears treated by radiation in this study, the following was observed:

a) Eight ears with perceptive hearing losses remained so without much shift; six ears became worse, averaging 12 db loss; four ears improved 10 db pure tone (this involved two subjects who displayed improved bilateral hearing).

b) Three ears with conductive losses did not change under treatment, while two ears developed larger conductive losses, approximately 10 db.

c) Differing from those cited above, three individuals had their perceptive losses converted into a mixed conductive loss by radiation which depressed the air conduction line approximately 20 db. On the other hand, there was one individual who had his air-bone gap

eliminated by radiation which converted his hearing into a perceptive loss and also lowered his over-all hearing by 20 db.

There is a differential effect as to frequency. The 4000 cps frequency range shows a greater deficit in hearing capacity than any of the other frequency response areas. On the other hand, the area least affected appears to be in the region of the 2000 cps tone. From test to test, during radiation therapy, the response to the 4000 cps tone showed more variability than the responses to other frequencies. In this regard, it is noted that the greater loss for the 4000 cps tone is associated in almost every case, with a conductive component which might also account for the variability in the test results for this tone.

The shift in speech reception was small and correlated well with the over-all change in response to pure tones with the exception of some few cases which were drastically affected, losing as much as 21 db of speech reception threshold, more than the pure tone threshold. Despite this, discrimination did not appear to be affected.

On the basis of this study it is concluded that when an original perceptive loss of acuity becomes greater under treatment, this is primarily due to the development of a conductive component, which appears directly related to the radiation induced changes in the middle ear.

Recruitment was one of the factors investigated. This phenomenon is generally regarded as evidence of cochlear deficit. However, recruitment was observed to occur on a temporary basis in this study. From test to test during the period of therapy a number of patients developed various degrees of recruitment most of which disappeared after the radiation was completed. Significant to the experiment was the observation that the recruitment appeared to fluctuate in degree and from frequency range to frequency range as therapy continued. Generally recruitment due to radiation disappears at the end of treatment so long as it was not present before therapy began, and remains if it was present before treatment. Four of the subjects developed tinnitus during radiation therapy, but this was not studied further.

COMMENT

While recent investigation by several authors seems to confirm that there are no microscopically demonstrable changes in the cochlea and labyrinth during or shortly after irradiation,[1,2] definite changes can be detected later in the surrounding bone, blood vessels, connective

tissue and ossicles. In the light of these pathologic changes, correlation can be drawn with the present audiologic findings.

The epithelial lining of the mucosa covering the middle ear structures is desquamated by cancercidal doses. Edema of the mucosa and the collection of sterile fluid in the middle ear are not uncommon. Moss[8] termed this process "radiation otitis media." This is responsible for the conductive loss. Rarely bacterial invasion of this fluid collection may complicate the picture with the actual development of a purulent otitis media.

Radiation induced changes in the structures surrounding the end organ of hearing includes vascular and connective tissue alterations. These changes in the environment may not be manifest for years, but which later eventually can affect the end organ itself. This will eventually result in a perceptive type of hearing loss due to chronic anoxia. The collagen and the smooth muscles in the wall of the small blood vessels degenerates and undergoes swelling. The swelling of the endothelial cells may narrow or close the lumen of small vessels or enhance the formation of the thrombi. This obliterating endarteritis may seriously impair the blood supply to the cochlea, labyrinth or ossicles. The ossicles may undergo radiation necrosis if the blood supply is cut off. This may result in a conductive hearing loss. The major vessel to the outer ossicles is a branch of the anterior tympanic artery.[9] The network of vessels in the mucosa surrounding the capsule of the incudo-stapedial joint also supplied by branches of the superior and inferior tympanic arteries. The blood supply of the long process of the incus is known to be particularly meager. Gyorkey and Pollock[10] reported recently a case of progressive hearing loss following radiation. Surgical exploration of the middle ear revealed that the long process of the incus was replaced by a fibrous band. These changes were considered by these authors as the end result of an aseptic necrosis due to the radiation effect on the vascular supply of the long process of the incus.

While these changes in the ossicles were secondary to the diminished blood supply, mature bone is fairly resistant to radiation. Acute radio-necrosis of the bone is generally caused by a single, large dose. Frey[11] in 1956 used 5000 r in a single dose to irradiate the femur of guinea pigs and this resulted in osteolytic necrosis. Patients treated for head and neck tumors receive large, but fractional doses without evidence of acute changes in the temporal bone. However, the periarteritis and endarteritis, which follow radiation might lead to damage of the organic components of the temporal bone due to insufficient

circulation. On the other hand, this radiated bone tissue shows a decreased resistance against infecting organisms. Block[12] reported a case where the radiation of the temporal bone resulted in osteomyelitis of the bone several years after the radiation was completed.

Necrosis and breakdown of the skin of the external ear canal with or without secondary infection is less frequently seen during or following CO 60 treatment compared to conventional x-ray.

While the permanent pathologic changes can be easily studied at post-mortem examination, only the disturbed function indicates acute pathologic alterations in the hearing organ, which at times may completely clear up and the organ returns to its normal function. Since definite and characteristic microscopic changes in the cochlea and labyrinth cannot be demonstrated during or shortly after radiation, it can be assumed that the observed disturbances in the performance of the hearing apparatus are most likely due to radiation induced temporarily, physico-chemical changes in the cochlea, in the transmitting nerve elements or in the central nervous system. Thus the recruitment phenomenon which is considered as an evidence of cochlear deficit, was prevalent in a fairly large percentage of our cases; however, it was not a constant finding. It usually subsided in a few weeks after the radiation treatment was over. We do not have a definite explanation for this. Temporarily increased peri- or endolymphatic pressure due to increased permeability of blood vessels in the cochlea; changes in the permeability of the cells of the cochlea; disturbed metabolism of the cells of the cochlea are hypotheses. The first of these hypotheses seems to be supported by the findings of Vogel, et al.[13] who exposed monkeys to 10,000 r of high intensity gamma radiation. This caused a transitory vasculitis and choroid plexitis. These lesions were established within two hours after radiation. Inflammation was scant in the choroid plexuses of animals sacrificed after 24 hours. There were no consistent structural alterations in the collagen or elastica of the choroid plexus or other blood vessels. Upon this analogue, we may assume that similar changes in the blood vessels of the stria vascularis and the arachoroid mesh in the perilymphatic space could be responsible for temporary increased intralabyrinthine pressure which soon disappears after the radiation treatment is over.

SUMMARY

Fourteen patients receiving between 4000 r and 6000 r radiation at the region of the cochlea were studied. It was observed that the

radiation affected individuals selectively by generally causing a small shift in hearing threshold. This shift appeared to be primarily due to the development of a "radiation otitis media." No changes were observed in a considerable number of ears examined. The appearance of perceptive hearing loss and temporary recruitment is thought to be related to a transient vasculitis in the inner ear. The disturbed function of the cochlea is probably the result of an altered metabolism of the hair cells or an increased endo- or perilymphatic pressure due to the transient vasculitis.

It seems to be generally agreed by several investigators who studied this subject recently that ionizing radiation in the dose used for head and neck tumors does not cause microscopically detectable changes during the course of treatment in the cochlea or labyrinth.[1,2] The late effects of radiation are related to changes in the collagen, blood vessels and bone and are a separate entity.

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XXII

THE PROGNOSIS AND TREATMENT OF
CAVERNOUS SINUS THROMBOSIS

REVIEW OF 878 CASES IN THE LITERATURE

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Since 1950, many reports of survivals of cavernous sinus throm-
bosis have appeared in the literature. In some circles the opinion has
been voiced that this disease no longer bears the grave prognosis as
in the pre-antibiotic era. The purpose of this report is to dispel this
complacent thought and to make a definite statement as to the prog-
nosis and treatment of this serious condition.

The history of this disease has been recorded in the literature and
does not require repeating. Its pathogenesis is variable and has been
well described by Pratt[1] and others. Hager[2] gives one of the best
discussions on the pathological findings. These are matters of record
and will not be dealt with in this short paper.

It is only in recent years that attention has been drawn to this
disease by the number of cures reported by various authors. In 1950,
Pirkey[3] found 107 survivals in the literature. Most of these were
reported in the ten year period prior to 1950, as very few are found
prior to 1940. In his studies, Lillie (1951)[4] could find only two sur-
vivors in the ten cases which occurred at the Mayo Clinic from 1919
to 1951. Shaw (1952),[5] in commenting on the number of survivals
reported, stated, "This gives an over-optimistic picture, since recoveries
are more frequently reported than fatalities."

Considering the lack of any large series of reported cases in the
literature, it is no wonder that no one has yet ventured an opinion as
to the prognosis of this disease. Indeed, the largest series yet recorded,
is that by Grove (1936)[5] which lists 400 fatalities. Therefore, it
would seem reasonable to review the literature on this disease in an
effort to present a realistic picture of the prognosis and the most effec-
tive forms of treatment.

From the Rochester General Hospital, Rochester, New York

In my review of the literature I have found 878 cases of cavernous sinus thrombosis. These cases include 640 recorded fatalities. Of the 238 survivals, only 202 were followed up after initial recovery. Of these patients, 132 showed residual pathology which caused permanent disability of variable degrees. This series shows a mortality rate of 72.8% and a morbidity rate among survivors of 65.3%. In comparing these figures with those of other authors one finds general agreement. Previously reported mortality, in small series, have been: Eagleton[8] 88%, Lillie[4] 80%, Shaw[5] 92.5%, and Yarington[9] 75%. The 100% mortality rate given by Grove (1936)[6] and Dixon (1926)[10] are not to be considered due to their early date. I have previously estimated the morbidity at 88%,[9] based on 60 cases reported by Shaw (1952).[5] In general, based on the previously reported small series and the present series of 878 cases, a mortality figure of 80%, with morbidity at 75%, seems a realistic prognosis for this disease. One must realize that any figure arrived at is, of necessity, conservative, as many fatalities and undiagnosed cases are never reported.

The danger of misdiagnosis in cavernous sinus thrombosis is not widely recognized. It is not infrequent, however, that one finds this condition, on autopsy, in patients diagnosed as cerebral vascular accidents, severe facial cellulitis, chronic sinusitis, acute ethmoiditis, or generalized septicemia. Eagleton's[8] criteria: generalized sepsis; venous obstruction of the retina, conjunctiva, and eyelid; paresis of the third, fourth and sixth cranial nerves; meningeal irritation; and proptosis, should bring the diagnosis within the scope of any physician.

The treatment of patients suffering from this disease should be prompt and energetic. The type of therapy and the clinical course will be demonstrated by the following case history.

An 11 year old girl was admitted to a hospital with a 36 hour history of a pustule on the inner canthus of her right eye, accompanied by headache, lethargy, and some disorientation. She had bilateral periorbital cellulitis, proptosis, orbital edema, and ophthalmoplegia. Her temperature was 105° F., pulse 120, respirations 36, and her blood pressure 110/60. She had crepitant rales in both lung bases with no dullness to percussion. Her heart showed sinus tachycardia with no murmurs. She had a positive Babinski sign on the right, nuchal rigidity, hypoactive deep tendon reflexes, and generally spastic movements. The rest of her physical examination was essentially negative.

A spinal tap showed a pressure of 350 mm water with cloudy fluid, 2300 white blood cells per mm³, 116 mgm/100 ml of protein, 84

mgm/100 ml sugar, and 590 mgm/100 ml chlorides. Stain and culture for bacteria were negative. A blood culture grew coagulase positive staphylococcus.

A therapeutic program of 100 million units of penicillin and 6 gm sulfadiazine intravenously, 2 gm chloromycetin orally, and 3 gm streptomycin intramuscularly every 24 hours was begun.

The patient responded with a drop in temperature to 99° F., but a tachycardia of 180 per minute developed. She had five severe episodes of epistaxis which responded to packing, Adrenesin, and one pint of whole blood. She became comatose 12 hours after admission and never regained consciousness. Her bronchopneumonia became more advanced and respirations labored. Gross hematuria and paralytic ileus developed on the third hospital day, and a tracheotomy was performed to avoid further respiratory distress. The child expired in the early hours of the fourth hospital day. The eye signs remained the same throughout the course of treatment.

Although this patient did not survive, the treatment was adequate, according to the recommendations of most authors. Albrecht has reviewed 39 cases in which either penicillin or sulfa drugs or both were used, and has concluded that a combination of the two offers the best hope for survival. Most authors utilize one of the broad spectrum antibiotics as well.

The one element of treatment concerning which all are not in agreement is the use of anticoagulants. A brief look at the literature will show that it is only in recent years that anticoagulants have been used in dosages of any therapeutic value. Taylor[11] has reviewed this form of treatment and concluded only that there exists no good reason for not using heparin. Boies[12] recommends its use, while Kelley,[13] McAllen,[14] Shaw,[5] Pirkey,[3] and Lillie[4] do not. In my review, I can find no statistical support for its use, although it is of value as a prophylactic measure. On the contrary, the presence of cerebral hypertension, epistaxis, and orbital hemorrhage, so often seen in this disease, would seem to contraindicate the use of anticoagulants. At present, studies are being made to determine the value of the various fibrinolytic substances in the treatment of this condition.

SUMMARY

Eight hundred and seventy-eight cases of cavernous sinus thrombosis were reviewed in the literature and the mortality rate was esti-

mated at 80%, with morbidity of 75% among survivors. These figures are deemed conservative due to the number of unreported fatalities and undiagnosed cases. The treatment and clinical course are demonstrated by a case history and discussed. The use of anticoagulants is not advocated.

630 RIDGE ROAD EAST

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XXIII

EPISTAXIS SECONDARY TO SUBMUCOUS
RESECTION OF THE SEPTUM

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The operation of submucous resection of the nasal septum was originally described in 1884.   Prior to this time the septum was perforated in an attempt to increase nasal breathing or a turbinectomy was performed.   It was not until 1905 that this operation gained any degree of popularity.   Since this time numerous complications have been described in the literature and standard textbooks.   In a detailed search of the literature since 1917, only two cases of hemorrhage have been reported and both of these were of only moderate bleeding.   The following case history is submitted in which 36 units of blood were required prior to the control of a nasal hemorrhage secondary to a submucous resection.

The two initial cases reported were briefly: 1) in the USA in 1918, a 50 year old patient who bled until he went into shock.   A bleeding site was seen at the lower end of the incision.   The treatment consisted of subcutaneous horse serum and saline rectally.   He recovered.   2) In Germany in 1932, a 32 year old patient hemorrhaged on the tenth postoperative day.   The site of bleeding was not determined.   As the bleeding could not be controlled from anterior and posterior nasal packing, an emergency ligation of the external carotid artery of the involved side was performed.   The hemorrhage continued unabated.   It finally stopped spontaneously and the patient survived.

REPORT OF A CASE

This patient was a 22 year old healthy white male with a history of difficulty breathing through his nose.   The patient was asymptomatic until ten months prior to admission at which time he was allegedly struck in the nose and has been symptomatic ever since. At the time of trauma the patient had a profuse epistaxis which was controlled without medical intervention.

Past history revealed no bleeding tendencies having had several recent tooth extractions without abnormal bleeding.

The physical examination was entirely within normal limits except for a compound deviation of the nasal septa.

The hospital course consisted of a submucosal resection of the nasal septum performed under local anesthetic. There were no unusual complications other than a small perforation on the right side of the posterior nasal mucosa along the floor. As is our custom the anterior vaseline nasal packing was removed on the second postoperative day. At this time a small amount of fresh blood was noted. This came from the left side and was readily stopped with a single cotton pledget. Later in the evening of the same day there was a sudden onset of brisk bleeding of approximately 300 cc of blood necessitating a posterior and an anterior nasal pack. There was no further bleeding for six hours at which time bleeding occurred through the nasal packing. The patient went into syncope and was transferred to the recovery room. There the administration of a plasma expander was begun and several units of banked whole blood were given. During this first episode of bleeding the hemorrhage would be controlled from six to eight hours followed by another large hemorrhage and another secure anterior and posterior nasal pack. The bleeding was controlled after three days from its onset by repeated packing and after administration of eight units of whole blood. The patient had a mild febrile reaction after the eighth unit. The nasal packs were removed 24 hours after bleeding was controlled and the patient was returned to the ward. Three days later on the eighth postoperative day there was a spontaneous hemorrhage again requiring insertion of packs and additional units of blood. The patient was again taken to the recovery room and placed on the seriously ill list and his progress was even more carefully observed. During the first 24 hours of the second episode, the nose was repacked on several occasions but we were unable to compltely control the hemorrhage. The bleeding site was not observed, but in general the bleeding came from the superior posterior aspect of the left nostril. Emergency medical consultation was obtained but no hematological abnormality was found in clotting time, prothrombin, prothrombin consumption, fibrinogen, platelets or peripheral smear. The only abnormality was an increased bleeding time which was normal when repeated 24 hours later. A general surgical consultation was obtained and it was jointly decided that ligation of the external carotid artery would probably not control the bleeding. Therefore, it was elected to maintain the nasal packs and transfuse as needed by following the hematocrits

every eight hours. Accordingly cut-downs were placed in both legs. Despite repacking on several occasions, using gelfoam and topical thrombin, hemorrhage was not adequately controlled. Numerous conversations were held with specialists in New York City, none of whom had ever handled a similar situation and had nothing further to offer. A consulting otolaryngologist surgeon saw the patient and on the twelfth postoperative day packed the posterior nasal cavities using a "carrot" nasal pack. He re-enforced this with a vaseline pack anteriorly. Following this procedure, there was no major hemorrhage. Two days following this packing, a neurosurgical consultation was obtained and recommendations included obtaining a cerebro-angio-gram to exclude the possibility of a vascular anomaly. This was done and the films were interpreted as normal. By the fourteenth post-operative day the bleeding was minimal and the hematocrit was nor-mal, stable and the patient had received 36 units of blood. During the latter part of the second hemorrhage, he developed high fever from a purulent sinusitis which was controlled partly with antibiotics but which subsided spontaneously following removal of the packs. The packs were then carefully removed over the next four days and no further bleeding was noted. The patient was returned to the ward and begun an gradual ambulation and regular diet. Liver func-tion studies at one month and six weeks postoperatively were inter-preted as within normal limits. The latter were obtained to provide a baseline for the possible development of serum hepatitis following multiple transfusions. The septum was examined and was noted to be intact despite the long period of compression packing.

CONCLUSIONS

From this and the brief review of the other two case histories, I draw the following conclusion: adequate anterior and posterior nasal packing will stop hemorrhages in the nasal cavity and nasopharynx. Also, a "desperation" ligation of the external carotid artery may be ill-advised. Should surgery be contemplated, the best anatomical sites would be a combination of 1) external carotid ligation above the superior thyroid artery, and 2) ligation of the anterior ethmoid arteries after they branch from the ophthalmic artery in the medial aspect of the orbit. This latter approach has been reportedly used successfully in severe epistaxis secondary to massive cerebral trauma where external carotid ligation alone had failed.

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XXIV

FOREIGN BODY EMBEDDED IN
RETROPHARYNGEAL SPACE

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AND

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The following case report is presented primarily because of the rarity of the condition and the number of intriguing problems encountered. No attempt is made to review the literature on this subject. It is sufficient to emphasize that a completely embedded large foreign body in the retropharyngeal space may not be a unique finding but is unquestionably a rare one. The only allusion to this condition which I encountered was a very brief description of two such cases by Jackson.[1,2]

Actually there is no limit to the type of foreign body which may be encountered in the upper food passage. To arrive at a diagnosis one is aided by the history, physical examination and radiographic findings. As a rule, most of the cases are handled with ease. On the contrary, it is possible for some of the cases to present a serious problem in the removal due to the position, location, shape or composition or both of the substance. Furthermore, there are times when there is a lack of correlation between the physical and roentgenological findings which can prove misleading unless properly interpreted.

REPORT OF A CASE

A 40-year-old white female was first seen at the Jewish General Hospital on August 26, 1959. The patient stated that three hours previously she had been eating a piece of chicken and while doing so believed that she had swallowed a chicken bone. She denied experiencing any episode of coughing or choking or vomiting or dysphagia or dyspnoea or cyanosis or stridor or hoarseness. Instead she described a somewhat bizarre sensation of a lancinating pain which was referred toward the nape of the neck. This piercing pain was only fleeting in nature and was promptly superseded by a distinct discomfort in

Fig. 1.—Lateral radiograph of neck - August 26, 1959. An opaque linear foreign body can be readily seen just anterior to the bodies of C3, C4, associated with slight soft tissue swelling.

the back of the neck precipitated by head movements, especially by lateral rotation to either side. She did admit attempting to dislodge the alleged chicken bone by ingestion of crusts of bread but emphatically denied introducing her finger into her mouth at any time.

PHYSICAL EXAMINATION (CLINICAL)

The patient was robust with a good color and in no apparent pain except for the discomfort already mentioned on head movement. No subcutaneous emphysema was noted.

The otolaryngological examination included a search of the nose, mouth, fauces, pillars and tonsils. She was in full possession of her own teeth. Under local anesthesia a mirror examination was made of the postnasal space, the base of the tongue, the supraglottic structures, the larynx, the piriform sinuses and the postcricoid area. The positive findings encountered included a red irritated edematous posterior pharyngeal wall, probably more pronounced on the right side, and the swelling of the arytenoids. No abrasions or lacerations

Fig. 2.—Lateral radiograph of neck - one day later. Shows the foreign body as before: It is associated with more soft tissue swelling and appears to have moved slightly craniad.

could be detected anywhere in the pharynx. The lung fields were resonant to percussion and normal breath sounds were heard by auscultation. No wheeze could be heard.

Bearing in mind that the anamnensis could be faulty and possibly misleading, I (P.I.) was nevertheless intrigued by the peculiar type of pain and discomfort she described. To ascertain the cause of the edema of the posterior pharyngeal wall posed further embarrassment. Hence, the next step was to seek radiological aid.

RADIOLOGICAL EXAMINATION

The lateral radiograph of the neck was extremely valuable. It revealed a foreign body approximately 3 cm in length completely embedded in the retropharyngeal space at the level of C3 and C4
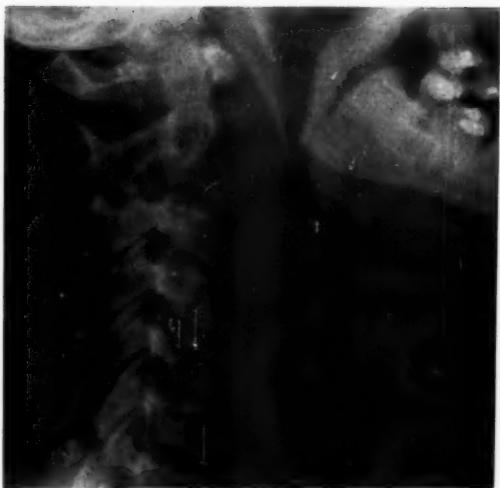
Fig. 3.—Lateral radiograph of neck: four days after original film. There is increased soft tissue swelling.

Fig. 4.—Foreign body.

associated with a slight retropharyngeal swelling (Fig. 1). A careful study of the A-P projection did present an indistinct shadow which was assumed to represent the foreign substance.

ENDOSCOPIC EXAMINATION

Under general anesthesia an examination of the entire pharynx with an esophageal speculum failed to disclose the point of entrance of the foreign body. Because of the marked swelling of the posterior wall of the pharynx the foreign body could not be palpated.

Once the diagnosis was established consultation with a view to therapy was deemed desirable. It was agreed to put her on expectant

therapy along with sterile fluids by mouth and antibacterial therapy. Lateral radiographs taken one (Fig. 2), two and four (Fig. 3) days later respectively demonstrated the same shadow with increasing retropharyngeal cellulitis. On August 31, 1959, a second confrere joined us in consultation and on this occasion surgical intervention via transoral route was decided upon.

TOMOGRAPHY

The frontal projection revealed a curved foreign body approximately 32 mm in length slightly to the right of the midline, and overlying the bodies of C2 and C3. Thus, both the position and shape of the foreign body were elucidated.

OPERATION

Under intratracheal anesthesia a right paramedian incision of the posterior pharyngeal wall overlying the body of C2 and C3 was made. A careful dissection was carried posteriorly through the edematous tissues to the prevertebral fascia. A tedious search for the foreign body by a seeker proved of no avail. However, it was readily located by finger palpation in the inferior angle of the incision. After a little more blunt dissection the upper portion of the foreign body was exposed, grasped with a forcep and removed with ease (Fig. 4). The original incision was approximated with two interrupted plain catgut.

The patient made an uneventful recovery. The lateral roentgenogram of the neck taken three days later showed a diminution in the cellulitis of the retropharyngeal tissues. The previously described foreign body was notably absent.

SUMMARY

A case is presented of a chicken bone buried in the retropharyngeal space. It was removed by a pharyngotomy through the transoral approach. It was unusual because of the location of the foreign body, the absence of the anticipated history, the lack of an upper denture and the association with a bizarre type of pain and discomfort.

CONCLUSION

Each foreign body presents a different problem which must be solved in its own appropriate fashion.

1538 SHERBROOKE ST.

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2. Jackson, C.: Peroral Endoscopy and Laryngeal Surgery. St. Louis, Laryngoscope, 1915.

Soon after the completion of this presentation the following case report was noted:

3. Cranmer, L. R.: Foreign Body of Retropharyngeal Space. Arch. Otolaryng. 70:793 (Dec.) 1959.

Abstracts of Current Articles

EAR

Early Diagnosis of the Glomus Jugulare Tumors of the Middle Ear

Van Eyck, Marcil: Annales D'Oto-laryngologie 77:7-8:595-598, 1960.

These tumors originate from the glomus bodies which are frequently located in the adventitia of the dome of the jugular vein and, also, along the ramification of Jacobson's nerve to the promontory. The clinical symptoms depend on the location of the tumors. Those developing in the adventitia of the jugular dome produce late symptoms; if the tumor originates in the middle ear, early auditory and vestibular symptoms are evident.

Five cases were seen by the author; three cases, because of early diagnosis, are presented. The first case showed vertigo, hearing loss and epileptic seizures. Tympanotomy revealed a pin sized tumor in the anterior inferior quadrant of the middle ear. The symptoms cleared following its removal. The seizures were explained by the presence of the tumor over the sympathetic system of the carotid. The second and third cases also had vertigo and tinnitus which were cured by the removal of the tumor.

The authors stress that early treatment of these tumors is necessary to obtain a cure. Exploratory tympanotomy is justified in cases presenting unilateral conductive hearing loss, tinnitus and vertigo.

GOZUM

Observations of Intravenous Administration of Substances 22 and 4099 in Cochleovestibular Syndromes of Vascular Origin

Bouche, J., and *Freche, Ch.*: Annales D'Oto-laryngologie 77:6:498-503, 1960.

The authors review the role of cholesterol in the pathogenesis of atherosclerosis, and point out that exogenous cholesterol constitutes only 20 per cent of the total cholesterol. The remainder is produced in the liver. They assume atherosclerosis may develop in three stages:

I—Disturbance in the control of cholesterol by different hormonal and alimentary factors.

II—Disturbance in the plasma colloids as a result of large lipid molecules.

III—Precipitation of cholesterol and lipids in the intima of the arteries. 22th and 4099 are simplified derivatives of the biliary acids.

Their action is due to the blockage of the coenzyme.

The authors believe that most of the cochleovestibular syndromes are due to atherosclerosis of the branches of the internal auditory artery. They used these drugs on 59 patients by intravenous injection with the idea of modifying endogenous cholesterol synthesis. Cholesterol level fell in 80 per cent of the cases, vertigo disappeared in 75 per cent, and tinnitus improved in 65 per cent. Hearing improvement was subjective, no audiometric results being reported.

Gozum

Studies on Cholinesterase of Labyrinthine and Spinal Fluid

Kato, T.: J. of Oto-rhino-laryng. Soc. of Japan 63:1 (Jan.) 1960.

In view of the importance of acetylcholine and cholinesterase on the mechanism of sound stimuli transmission, the author studied the cholinesterase (ChE) activity of the labyrinthine fluid of guinea-pigs and the human spinal fluid.

He adopted Conway's microdiffusion analysis by experimental study on guinea-pigs and Hesterin's method with Beckman's spectrophotometer by clinical study on the patient.

The results obtained were as follows:

1. ChE in the labyrinthine fluid, both in endolymph and perilymph, was specifically related with nerve-muscle function.

2. ChE activity of endolymph was 4.36 times higher than that of perilymph.

3. The injection of 2% quinine hydrochloride solution decreased gradually the ChE activity of endolymph and perilymph in parallel values.

4. The injection of dihydrostreptomycin decreased the ChE activity more remarkably and earlier than quinine.

5. A sound exposure (3000 cps, 90 db for 60 hours) diminished markedly the ChE activity of labyrinthine fluid and that of the endolymph appeared inhibited completely.

6. In human spinal fluid the normal ChE activity was 0.175 ± 0.006 Elog I_0/I in equilibrium at range $\lambda 500m\mu$, the upper limit was 0.200 and the lower limit was 0.140.

7. In 11 cases of conductive deafness, the ChE activities were normal or slightly below normal except in 2 cases of acute suppurative otitis media.

8. In 19 cases of nerve deafness, a considerable diminution of ChE activity was observed except in 2 cases. In deafness due to detonation, traumatic, streptomycin, Meniere's syndrome, following a cerebral abscess and in congenital deaf-mutism, the ChE activity decreased remarkably.

HARA AND OGURA

Fenestration of the Oval Window—Four-Year Report

Shea, J. J., Jr.: Jour. Amer. Med. Assn. 174:2181-2186, 1960.

The author discusses his surgical technique for otosclerosis, in which the entire stapes is removed and a fenestra created in the oval window by saucerizing the otosclerotic margins with a 0.4-mm cutting burr. A vein graft averaging 3 by 4 mm and less than 0.005 in. thick is placed over the fenestra, and the stapes is replaced by a polyethylene-90 strut, usually 4 mm long. He has used this technique in 1400 patients, has not changed it in the last two years. In 14 patients the hearing worsened; 6 of these had had prior stapes mobilization which he opposes. Ninety-four of 100 patients maintained an air-bone closure within 10 decibels for more than one year. He feels more conservative procedures will eventually fail in the younger patients. Although he had a 0.5% incidence of total hearing loss, he feels this would have been higher, had he not avoided the trauma to the cochlea from chisels as some advocate.

TRIBLE

1. **Conservative and Surgical Management of Meniere's Disease, Including a Critical Evaluation of Its Pathogenesis**

   Wustrow, F., and *Borgowsky, B.*

2. **Meniere's Disease and the Diencephalic Regulatory Function**

   Rossberg, G.

3. **Dichotomy of Auditory Threshold, Functional Change, and Tonal Dedifferentiation in a Case of Meniere's Syndrome**

   Rabending, G.

4. **A New Observation Concerning the Histopathology of Meniere's Disease**

   Busanny-Caspari, W., and *Matzker, J.*

5. **Transtympanal Injections as Treatment of Meniere's Syndrome**

   Kroath, F.
   Z. Laryng. Rhinol. 39:133-194, 1960.

The March issue of the (German) Z. Laryng. Rhinol. contains five papers devoted to various aspects of Ménière's disease.

The first article (Wustrow and Borgowsky) compares the results of conservative management with that of destruction of vestibular

function either by surgery or by the use of streptomycin. The authors report that in their hands 66% of patients are at least "improved" by conservative measures alone. With reference to the refractory group, they maintain that "mild" cases are frequently better off with an occasional attack than with the permanent disability (feeling of unsteadiness) which may or may not be induced by surgery. Moreover, in many of the mild cases, the attacks subside entirely with time. The authors, therefore, consider destructive measures as methods of last resort. The use of streptomycin is recommended in bilateral cases only. Surgery is reserved for those severe cases in which patients are practically disabled by their condition. Intracranial nerve resection is recommended for all cases in which the auditory function is considered worth saving. However with the auditory function already gone, vestibulotomy is indicated.

The second paper (Rossberg) is an inquiry, largely theoretical, into the possible causes of Ménière's disease. The author attempts to classify the disease as a disturbance of the autonomic nervous system. This is explained by analyzing two other diseases which are apparently better understood in this connection: epilepsy and migraine. A characteristic triphasic chain of events is said to occur: 1) disbalance of the autonomic system, due to failure of the diencephalic regulatory

mechanism, with one of the two component functions becoming dominant; 2) over-compensation in the direction of the other component; 3) re-establishment of normal autonomic balance. If the component under 2) happens to be the sympathetic system, a systemic reaction is to follow of which an epileptic attack is said to be a typical example. In the other case, i.e., when the parasympathetic is involved in phase 2), the reaction may be confined to a single organ because of the relative autonomy of peripheral parasympathetic nerves. Migraine is said to be typical of this latter group. By fitting various symptoms associated with Ménière's disease into this general scheme, the author explains Ménière's disease as a case of the second class, i.e., parasympathetic over-compensation after an initial disbalance of the autonomic system in which the sympathetic system was dominant.

The third paper (Rabending) reports on audiometric findings in a patient with Ménière's disease. As is well known, most critical listeners report a dichotomy of their sensation when the threshold for pure tones is tested: at first they are able to detect sounds like a noise. From it the tonal character of the test tone gradually emerged on further increase in intensity. This phenomenon was seen in a Ménière patient on the involved side only. Furthermore, when this patient was exposed to a (supra-threshold) pure-tone signal, it gradually assumed the character of a noise again. The remainder of the paper attempts an explanation of this finding in which, in addition to auditory-physiological terms, phrases like "Gestalt"-Psychology figure quite heavily. The author is a psychiatrist.

The fourth paper (Busanny-Caspari and Matzker) concerns a histo-pathological finding. During the course of a labyrinthine destruction for a severe Ménière, the horizontal membranous canal was removed almost in toto. While still in situ, the membranous canal did not give the impression of a hydrops. Histologically, the basal layer was thickened and had undergone hyalinization. Parts of the wall were edematous with vacuoles present in the epithelial layers. Small amounts of hemosiderine were found in some parts of the tissue.

The authors stress the point that their material was collected during the course of an active disease. (Patient suffered an acute attack while on the table.) The question is raised whether the endolymphatic hydrops found in autopsy material *after* Ménière's disease by a variety of authors might not be the final manifestation of a degenerative process of which their own finding then represents an earlier stage. (The authors are apparently unaware of the paper by Lempert et al: Annals of Otolaryng. 61:717-749, 1952. Firstly,

Lempert had also collected his material during the course of larynthec-tomies. Secondly, Lempert had also reported on degenerative changes in his material. Thirdly, there is the question whether the epithelial vacuoles of the present authors and the "vesicles" of Lempert might not be one and the same thing. In that case, Lindsay, Altmann, and others have shown that these vesicles or vacuoles are a normal finding and were already known to the older anatomists in the middle of the nineteenth century. Rev.)

The fifth and final paper (Kroath) is a report on treatment and concerns transtympanic injections of hyaluronidase-novocaine. When given during acute attacks, the author saw the vertigo subside, while the auditory symptoms remained unchanged.

Finally, it ought to be noted that most of the authors subscribe to Altmann's view that Ménière's disease must not necessarily be equated with endolymphatic hydrops.

TONNDORF

Pathologic Mastoid Pneumatization Associated with Milk Allergy

Rauch, S.: Med. Welt 1442-1447, 1960.

The pneumatization theory of Wittmaack (1928) had held that the mucosa of the middle ear possesses an "agent" which promotes the development of the pneumatic system. Middle ear infections (i.e., acquired factors) occurring in early children, or even before birth, were thought to interfere with the activity of this agent, thus produc-ing abnormal forms of pneumatization.

Based upon his investigations in identical twins, Albrecht (1930) postulated that the activity of the tympanic mucous membrane was determined by genetic factors.

In 1950, the author of the present paper arrived at a conception which represents a compromise between these two opposing view-points: In experiments in guinea pigs, it was found that a combination of allergic reactions and of infections of the middle-ear mucosa, both artificially induced, affected pneumatization adversely. (Guinea pigs normally develop some, though small, air spaces adjacent to the middle ear.) Neither allergy nor infection alone produced this form of maldevelopment. Since the predisposition to allergic reaction is gen-

erally considered an inherited trait its combination with infections (i.e., acquired factors) presents indeed a compromise between Wittmaack's and Albrecht's viewpoints.

Albrecht had already referred to the potential role of "nutritional factors." In his material he had noted that many infants with low-grade pneumatization had been fed with cow's and other (foreign) milk. The author now raises the question whether a milk-allergy might have played a role in the maldevelopment of the mastoids of such children. After discussing the general problem of milk-allergy (author makes an attempt to pinpoint certain milk proteins as potential antigens), three clinical cases (infants) are presented in which otitis media and mastoid maldevelopment were associated with milk allergy. The author stresses the point that milk is only one of many allergic factors which might play a role in mastoid maldevelopment, although he thinks it may be a particularly good example for the demonstration of the combined effects of allergy and infection.

(It may be noted that the dispute: genetic vs. acquired factors is carried on very actively between M. Diamant, Halmstad, Sweden, and A. Tumarkin, Liverpool, England. Mr. Tumarkin considers himself a "Neo-Wittmaaackian." Rev.)

TONNDORF

X-ray Studies of Frontal Sinus and Mastoids in Neandertal Man of Middle Europe

Kindler, W.: Z. Laryng. Rhinol. 39:411-424, 1960.

This is an interesting attempt to contribute toward an understanding of the development of the pneumatic spaces, both paranasal and mastoid, by taking a look at man's older relatives. Examined were six skulls (or remnants thereof) considered to belong to the class of Neandertal man of the Mousterian period. This number is admittedly small. Moreover, in two of the cases x-rays could not be taken because of complete petrification of the specimens. Yet the similarity of the findings in the remaining cases suggests that both the frontal sinus as well as the mastoid air spaces were in a decidedly lesser state of development than that reached in modern man.

It is generally conceded that Neandertal man carried his head only in a semi-erect position. Furthermore, the external size of the mastoid of all known Neandertal skulls is notably small. Combining

these two facts, the author concludes that the muscular pull upon the mastoid process was small. This would support the concept that it is this muscular action which contributes to mastoid growth. (Although the author does not explicitly state so, he seems to favor the genetic theory of mastoid aircell formation. Rev.) The smallness of the frontal sinus appears to show that the large supra-orbital ridges so characteristic of early man consisted largely of solid bone, although some diploic spaces are recognizable in the x-ray pictures.

<div align="right">TONNDORF</div>

Causes of Recurrent Perforations of the Eardrum after Tympanoplasty

Kley, W.: Z. Laryng. Rhinol. 39:438-442, 1960.

The author divides these perforations into two classes: those occurring during the postoperative period of wound healing ("early" perforations)and those taking place after the healing was complete ("late" perforations). Both forms may have common causes: tubal and hematogenic infections, allergy, and trauma. However, the main cause of "early" perforations lies in surgical failures, e.g., too excessive thinning down of the transplant, or graft necrosis due to insufficient blood supply, or failure of the graft to take at its margins. Among the causes of "late" perforations are epithelial and seborrhoic cysts, including graft cholesteatoma according to Zoellner and Beikert (cf. abstract this journal: ANNALS OF OTOLOGY, RHINOLOGY AND LARYN-GOLOGY 67:1223, 1958); furthermore, ulcer- and granulation-forming dermatitis; and finally, what Wullstein considers, a failure of the graft to adapt itself to its new site. The author supports his thesis with the aid of photomicrographs of histological sections of some representative cases.

<div align="right">TONNDORF</div>

Osteochondrosis of the Temporo-Mandibular Joint

Feist, J. R., and *Gibbons*, T. G.: Radiol. 74 (Feb.) 1960.

Osteochondromatosis arises from the synovial membrane and may consist of one or more osteocartilagenous bodies not related to adjacent bony parts. A case of osteochondromatosis of the temporomandibular joint is presented. Roentgen examination revealed the presence of

two calicified bodies associated with the joint. The laminagrams revealed them clearly. One was excised and proved to be osteo-cartilagenous. The authors emphasize that patients with pain and limitation of motion of the temporomandibular joints who continue to have symptoms not fully explained by conventional radiography are candidates for laminagraphic examination.

Five figures and five references are included.

JORSTAD

The Cause of Discontinuity of the Long Crus of the Incus

Mueller, E.: Z. Laryng. 39:313-316, 1916.

A discontinuity of the long crus of the incus is a relatively frequent finding during the course of tympanoplastic procedures. In the author's experience, it was seen 18 times out of 100 tympanoplasties and radical mastoidectomies.

The possible causes of such occurrences have been discussed to quite some extent in the older otological literature at the turn of the century. The earlier view, that such lesions were the result of a bony caries was corrected by O. Mayer and H. Beyer in 1929. It is the consensus of opinion since then that losses of the long crus of the incus are due to the simultaneous occurrence of resorptive and productive osteitic processes.

The question posed by the present author concerns the basic condition(s) which may lead to such lesions. The author states that, as a rule, they are seen almost exclusively in cases of chronic suppurative otitis media. Histologically, there are two types which can already be distinguished in early infancy. In the first type, which is usually associated with normal pneumatic development, the incus represents a compact bone covered by a thin muco-periosteal layer. The second type shows a central marrow space which at some points may be so extensive as to be in direct contact with the periosteum. Usually, residual embryonic connective tissue is in evidence and pneumatization is poor. Quite often, the marrow space extends into the thin connection between the long crus and the lenticular process makes this quite a vulnerable point. The possibility of bacterial invasion of such bones during the course of an otitis media is quite obvious. Based upon his histological findings, the author considers the osteitis of the

ossicles actually a chronic osteomyelitis. This view is strengthened by the fact that middle ears with poor pneumatization, in which marrow-containing ossicles were said to be found, are prone to chronic infections.

In this otherwise informative article, the reviewer misses references to the work by T. H. Bast and B. J. Anson. These authors have reported on repeated occasions that the incus is originally formed as a typical marrow-containing "long bone." Replacement of the marrow space by enchondral bone starts approximately at midterm. In view of these findings, Mueller's observations must be considered as a persistent embryological condition, which is entirely in line with his associated findings of poor pneumatization and residual embryological connective tissue.

TONNDORF

Experiments in Hearing

von Bekesy, George (Translated and Edited by F. G. Wever), 745 pp., 688 figs. McGraw-Hill Book Company, Inc., New York, 1960. Price $25.00.

"Experiments in Hearing" covers Bekesy's work from 1924 to 1958, that is, for a period of 34 years. With a few minor exceptions, the book is a compilation of Bekesy's published papers. There is no doubt in the mind of this reviewer that these papers as a sum total represent the most important contributions in the field of audition made in our times. Therefore, anyone interested in audition must want to own a copy. He will make constant reference to it for many years to come.

The lack of such a book was keenly felt by anyone interested in the field of audition, for about the first half of Bekesy's papers were originally published in German and, moreover, some of these were difficult to obtain. Prof. E. G. Wever must be highly commended for his endeavor in translating these earlier articles. After comparing the original with the translations on a few samples selected at random, this reviewer was impressed with Professor Wever's achievement. These translations are decidedly above the level of the ordinary "professional" translations. They display a congenial understanding of the subject matter.

Most of the papers are given verbatim although not in their original chronological order. They are grouped under three general head-

ings: 1) Conductive Processes; 2) Psychology of Hearing; and 3) Cochlear Mechanism. This grouping will facilitate orientation for the benefit of the reader. A cross index is provided since each paper listed in the bibliography carries a reference to where it may be found in the book. Viewed in this contextual order one cannot help being impressed by the magnitude of the work and by the stringent logical order in which these studies were pursued.

A fourth (introductory) chapter is devoted to the experimental approach. It is again put together from appropriate portions of published papers with only one single item added which was hitherto unpublished. This chapter contains sections on anatomical preparations (of what Bekesy calls "micro-anatomy," which lies between gross-anatomy and histology), on measuring techniques, and on the various tools developed for the latter purpose by the author himself. It is perhaps this chapter which reveals most clearly Bekesy's scientific method. This method is neither purely deductive because when Bekesy started his work there was not enough of a framework from which one could derive general hypotheses, nor is it purely inductive for a mere collection of data never makes up a new concept. For want of an accepted term, Bekesy calls this the "mosaic" approach. Its essence is in the diversity of attack: anatomical, mechanical, electro-physiological, and psycho-physical measurements combined with abstractions in the form of mathematical or physical models. All results finally fell into a common pattern (like the stones in a mosaic) and took on a broader meaning, thereby permitting the formation of general concepts. Such an approach calls constantly for the development of new measuring tools and techniques. The difficulties encountered can hardly be appreciated by the casual reader. This reviewer recalls a small incident which might illustrate this very point: Some years ago, when Bekesy first embarked upon his skin-analogy experiments he privately expressed his disappointment. For more than a year he had been beset by instrumental difficulties and had not made any progress on his original problem. A short time later, having mastered his difficulties, he published several experimental papers in rapid succession.

In summary, it may be stated that this book is not easy reading. It will prove to be most valuable as a reference book which should not be missing from the shelves of any man actively interested in auditory research. The amazing fact is that there is nothing dated about this book, even with regard to the earlier papers, although some concepts have been expanded since, either through Bekesy's own efforts or those of other workers in the field. Therefore, no major corrections

were needed in the preparation of the present edition. There is only one alteration this reviewer hopes will become necessary in future editions of this book: that it be expanded to include additional papers Dr. von Bekesy will have written between now and then.

TONNDORF

NOSE

Surgical Treatment of the Nasopharyngeal Fibromas

Radziminski, Aleksender: Annales D'Oto-Laryngologie 77:7-8:574-583, 1960.

The author reviews the literature for the treatment of nasopharyngeal fibromas and classifies these as physico-hormonal and surgical. Radium, x-ray therapy, electrocoagulation, and hormone therapy are included in the first group. The author comes to the same conclusion which is held by most European authors; surgical therapy is the treatment of choice for nasopharyngeal fibromas. Hormone therapy may be used in conjunction with surgical therapy. Objections to the surgical treatment are: disfigurement as a result of intervention, recurrences in spite of radical treatment and operative mortality.

Different surgical approaches are described as, transnasal, transbuccal, and transmaxillary; for large tumors the transmaxillary approach is suggested. The author prefers to operate under general anesthesia with controlled hypotention. Ligation of the carotid artery ipsilateral to the stalk of the fibroma is suggested, or ligation of the internal maxillary artery after removing the posterior wall of the maxillary sinus. Seven cases have been operated on by the author since 1953 without any complication.

GOZUM

Clinical and Histopathological Studies of Nasal Polyps

Yago, T.: J. of Oto-rhino-laryng. Soc. of Japan 63:154 (Jan.) 1960.

The author studied nasal polyps from the viewpoint of clinical findings, histopathology and relation to allergy.

Two hundred cases of nasal polyps were investigated concerning the relation to chronic sinusitis, allergic rhinitis and bronchial asthma; skin tests for allergy were done.

The result was that nasal polyps had a closer relation to chronic sinusitis than to bronchial asthma or allergic rhinitis.

But histopathological study of 102 specimens taken from these cases showed edema and eosinophilic infiltration which suggest a close relationship to allergy.

Therefore, the author considered that though the nasal polyp cases which showed allergic symptoms were few, there must exist some components of allergy.

Furthermore, the nasal polyp was proved to be of inflammatory origin rather than neoplastic by the author's investigation of the alkali-phosphatase reaction.

HARA AND OGURA

NASOPHARYNX

Nasopharyngeal Malignant Tumors: 82 Consecutive Patients Treated in a Period of Twenty-two Years

Eighty-two consecutive patients with malignant nasopharyngeal tumors verified histologically, were treated with irradiation from 1932 to 1954. Of these, 23 (28.2%) survived five years or longer. The 82 cases is 2.4% of the total cancer cases and 13.3% of the head and neck tumors treated during this period. Thirteen of these patients were Chinese and one Korean.

Cervical adenopathy on initial examination was absent in only 23 patients. Nineteen patients had initial involvement of cranial nerves. The disease remained unrecognized by patient and physician for an average of eight months.

Grossly, these tumors are ulcerated, lobulated or exophytic non-ulcerated. The difficulty of a completely satisfactory histologic classification of these tumors is discussed.

Treatment in general consisted of external and intracavitary irradiation to the primary and lymphatic drainage areas. Sixteen of the 23 patients without palpable cervical lymphadenopathy received no treatment to the cervical node areas. In 4 of these 16 patients cervical adenopathy subsequently developed. Thirty-four references and 9 tables are included.

JORSTAD

MISCELLANEOUS

"Premarin" as a Haemostatic Agent: Failure to Demonstrate Any Laboratory or Clinical Effect

Borchgrevink, C. F., Andersen, R., Hall, J., Hatteland, K., and *Ursin-Holm, A.:* Brit. M. J. 2:1645-1647 (Dec. 3) 1960.

The authors advised against the marketing of "premarin" as a hemostatic agent in Norway on the basis of this report. They found 1) no effect on various vascular, platelet, and clotting functions in normal individuals (nine type tests repeated over three hours in eight normal individuals), 2) no effect on prolonged bleeding time and positive tourniquet tests in five patients with a hemorrhagic diathesis, 3) no change in blood loss for three days in 31 patients undergoing prostatectomy compared with 40 controls, and 4) no effect on six patients with severe epistaxis compared with five similar patients on a placebo in a double-blind study.

They felt that even if a hypercoagulable state were produced, it would not necessarily be advantageous, and that there was danger in the false security of an ineffective hemostatic agent.

TRIBLE

Spent Radon Seeds: II. Radiation from Spent Radon Seeds

Johns, H. E., and *Skarsgard, L. D.:* Radiology 74:3:403-406 (Mar.) 1960.

Spent radon seeds from four patients were measured for radio-activity and tabulated. The method is described as for five spent radon seeds with an initial activity of 1.13 mc on September 16, 1933, and measured in December, 1958. Examination of tabulated results

indicate that the doses range from about 100 to 300 rads over the 10 to 20 year period. This dose is small and probably does not have too much significance. The possibility of its causing chronic irritation cannot be completely ruled out. Five references, three tables and one figure are included.

JORSTAD

High Energy Electrons in the Treatment of Malignant Tumors of the Thorax

Uhlman, E. H., and *Ovadia, Jaques:* Radiol. 74:265-272 (Feb.) 1960.

The authors' observations indicate that large doses of effective ionizing radiation can be applied to deep seated tumors with a relatively low integral dose to healthy tissue and consequent good tolerance by the patient. The cases treated were without exception in an advanced and inoperable stage.

Ten of 16 patients with carcinoma of the esophagus received a minimum of 6000 r to the lesion which at present is considered a satisfactory therapeutic dose. Rapid extension of the neoplastic process occurred in the other 6 patients and interruption of treatment became necessary. No serious complications occurred. The survival time of the 6 remaining patients is 1 for 19 months, 2 for more than 9 months and 3 for less than 6 months.

Twenty-two patients with carcinoma of the bronchus were treated. The majority remained ambulatory because the by-effects of electron therapy are mild and general condition of patient is little influenced. Local response to therapy was remarkable in all instances.

The authors believe this treatment of earlier diagnosed carcinomas of the esophagus and bronchus, is justified in preference to conventional methods of radiation therapy and surgery. Sixteen figures and 5 references are included.

JORSTAD

Perivascular Extravasation of Thorotrast

Brady, L. W., Chandler, D. E., Gorson, R. O., and *Culberson, J.:* Radiol. 74:392-398 (Mar.) 1960.

A case is presented in which six milliliters of thorotrast (colloidal thorium dioxide) was extravasated into the soft tissues of the left side

of the neck during attempted carotid arteriography. Ten years later a hard mass was palpable in the area of the neck and a Horner's syndrome with atrophy of the left half of the tongue had occurred. The calcified mass was removed with no increase in neurologic deficit and no progression occurred during 2 years since. In spite of the tissue dosage of 4000 to 5000 rads estimated to have been delivered over a period of 11½ years, there was no definite pathologic evidence of radiation effect. The findings represented a foreign body reaction. Seventeen references and 8 figures are included.

JORSTAD

Tumor Localization with Transverse Tomography: Diagnostic and Therapeutic Applications

Roswit, B., and *Unger, S. M.*: Radiol. 74:705-720 (May) 1960.

The authors describe their experience with transverse tomography for tumor diagnosis, tumor localization and prognosis, as an aid to improvement of the surgical and radiation treatment of malignant disease. In 9 cases by means of a total of 20 tomograms, 10 radiographs, 3 photographs and 3 line drawings they demonstrate the advantage of the tomogram in the treatment planning and how the tomogram is utilized in the treatment planning system. The authors emphasize that in localization for neoplasms of the head and neck transverse tomography can be truly helpful and occasionally even indispensable. Twenty-one references are included.

JORSTAD

Neoplasia Following Therapeutic Irradiation for Benign Conditions in Childhood

Saenger, E. L., Silverman, F. M., Sterling, T. D., and *Turner, M. E.*: Radiol. 74: 889-904 (June) 1960.

This investigation was initiated in 1956, in the Cincinnati area to determine whether or not radiation can be indicted as the principal causative factor in the induction of neoplasia following radiation exposure for either diagnostic or therapeutic purposes. A series of 1,644 persons of a total of 2,230, who were irradiated over the head, neck and chest in infancy and childhood, were compared with 3,777 siblings with respect to subsequent medical history.

Eleven carcinomas of the thyroid were found in the patient group, none were found in the sibling controls. The incidence of infections

was greater among patients than among their siblings. *The death rate in the siblings, however, was greater.

Although there is a significant increase in the incidence of cancer of the thyroid following irradiation, radiation does not seem to be the sole factor but rather contributory. In that the total family history was evaluated in this survey, the information obtained is extremely useful in placing in proper perspective possible carcinogenic factors other than radiation. Fifteen tables, 5 figures, and 23 references are included.

JORSTAD

Unilateral Hypertrophy of the Mandibular Condyle

Weissman, I., and *Collins, E. M.*: Radiol. 74:939-943 (June) 1960.

A proved case of hypertrophy of the right mandibular condyle with elongation of the vertical ramus of the right mandible, causing asymmetry of the face and malocclusion, is reported. A review of the literature revealed condylor hyperplasia to be well known in European clinics but Anglo-American authors consider it to be rare. Some of the etiologic aspects all discussed along with the major roentgenologic criteria necessary to establish the diagnosis. Three photographs, 5 radiograph, and 4 line drawings depict the findings.

JORSTAD

Bell's Palsy: Some Problems of Prognosis and Treatment

Dalton, G. A.: Brit. M. J. 1:1765-1770 (June 11) 1960.

The author investigated 98 cases of idiopathic facial paralysis seen from 1954 to 1956 at the United Birmingham Hospitals seeking criteria which might guide in predicting spontaneous recovery. Considering *associated symptoms*: all but 6 of 42 patients in whom there was only a facial paralysis made a complete recovery (and these 6 a partial recovery); only 26 of 44 patients presenting with facial paralysis accompanied by pain made a complete recovery, and 13 a partial recovery. Only 2 of 5 patients presenting with facial paralysis, pain, and auditory nerve symptoms made a complete recovery, and the other 3 a partial recovery. The remaining 7 patients presented with paralysis, pain, auditory symptoms, and herpetic vescicles (Ramsay Hunt's

syndrome) with 2 complete recoveries, 4 partial, and one made no recovery. The author concludes that the probability of complete recovery is lessened by the presence of pain, and much lessened if accompanied by auditory nerve symptoms and pain.

Associated branch lesions were investigated in each patient. The chorda tympani was tested by comparing galvanic effect on either side of the tongue; the stapedius branch was tested by the unpleasant effect of shrill noise, and the greater superficial petrosal branch was tested by comparing lacrimation and soft palate taste with electrodes. No correlation was found between branch lesions and prognosis except the only 2 patients with a dry eye failed to make complete recovery.

All 22 patients presenting with an *incomplete paralysis* made a complete recovery. The well known relation between duration of paralysis and prognosis was demonstrated: 59 of the 61 patients making complete recovery had begun to improve within 6 weeks.

The question of whether and when to decompress is discussed. Only 1 of the 4 patients decompressed after 8 weeks recovered all function. One with serum in the ear recovered after simple mastoidectomy. The author suggests more use should be made of cervical sympathetic block, "vascular decompression" by cortical mastoidectomy, and decompression of the nerve when electromyography indicates beginning nerve degeneration.

TRIBLE

Books Received

Cellular Aspects of Immunity

By *G. E. W. Wolstenholme*, O.B.E., M.A., M.B., M.R.C.P., and *Maeve O'Connor*, B.A., Editors for the Ciba Foundation. 8vo., pp. xii + 493, 117 illustrations. Boston: Little, Brown and Company, 1960. Price $10.50.

This symposium, with thirty-two participants from all over the world, shows that the immunologically competent cell rather than the antibody has become the central theme of immunology. The problems of how the cells are modified and influenced by immunological processes according to recent scientific observations are well documented. There is an excellent chapter on the ultra structure of antibody producing cells. Such studies are changing the definition and identification of cells from the traditional staining characteristics, to the ultra structures.

The clinician, as well as the researcher, will find this book absorbing and stimulating.

La Physiologie des Sinus

By *L. Flottes, P. Clerc, R. Riu* and *F. Devilla*, with collaborators. Paper, large 8vo., 592 pages, 253 illustrations and a color plate. Paris, 1960, Librairie Arnette. Price NF. 75.

This is the most complete collection of works on the physiology of the sinuses that we have seen. They are capably abstracted and reported and are embellished by the authors' own researches with the facilities of the Laboratoire de la Commission d'Etudes Pratiques des sous-marins. The anatomical basis is amply discussed and approximately 200 pages are devoted to therapeutic measures which are in harmony with physiological requirements. (In French)

Mikrozirkulation in der Nasenschleimhaut (Microcirculation in the Nasal Mucosa)

By *Prof. Dr. H. H. Naumann*, University Nose Throat and Ear Clinic, Würzburg. Paper, 8vo., 96 pages, 20 illustrations. Stuttgart, Germany, 1961. Price DM 18.60. (U.S. and Canada Intercontinental Medical Book Corporationn, N.Y., $4.45)

Highly recommended. The subject is treated under the general headings: Morphological background, Intravital microscopic observations, Pathological appearances, Physical chemical and therapeutic reactions in the vessels. 249 references.

Year Book of the Ear, Nose and Throat (Series 1960-1961)

Edited by *John R. Lindsay*, M.D., with a section on Maxillofacial Surgery, edited by *Dean M. Lierle*, M.D. and *William C. Huffman*, M.D. Cloth, small 8vo., 252 pages, 97 illustrations. Chicago, 1961. Year Book Medical Publishers, Inc. Price $8.50.

Maintains its usual high standard of selection and abstraction.

Manifestazioni Emorragiche in Otorinolaryngologia (Hemorrhagic Manifestations in Otorhinolaryngology)

By *Carlo Felice Porta*, *Gian Carlo Vidoni* and *Giacomo Maffei*, with the collaboration of *Luigi Migone*. Paper, large 8vo., 369 pages, 64 illustrations. Parma, 1960. Societa Italiana di Laringologia Otologia e Rinologia.

This work, although the consummation of a conference of the Gruppo O. R. L. Alta Italia, is presented in standard text-book form, comprehensive and well documented. (In Italian)

Notices

VII INTERNATIONAL CONGRESS OF OTORHINOLARYNGOLOGY

The Seventh International Congress of Otolaryngology will take place July 23-29, 1961, at Paris. The sessions will be held under the presidency of Professor Maurice Aubry at the New Faculty of Medicine, Rue des Saints-Pères.

Dr. Henry Guillon, Secretary General

6 Avenue Mac Mahon, Paris XVII, France.

AMERICAN OTOLOGICAL SOCIETY
The Lake Placid Club   May 26 and 27, 1961

PROGRAM
FRIDAY MORNING, MAY 26, 1961

1. The Differential Diagnosis of Vertigo Considered Bio-Anatomically

   Benjamin Spector, M.D.

2. Studies on the Efferent Innervation of the Vestibular End Organs

   Joseph Farkashidy, M.D. (by invitation), P. E. Ireland, M.D.

3. The Innervation Pattern of the Cochlear Hair Cells

   Catherine A. Smith, Ph.D. (by invitation)
   Discussor: Dr. Hans Engstrom

4. Pressures of the Labyrinthine Fluids, No. 2

   Francis L. Weille, M.D., John W. Irwin, M.D. (by invitation),
   Louise Clark, A.B. (by invitation), Phyllis Rahn, A.B. (by
   invitation)

5. Functional and Histologic Effects of Experimental Inner Ear
   Pressure Changes

   Brian F. McCabe, M.D. (by invitation), David A. Wolsk, Ph.D.

FRIDAY AFTERNOON, MAY 26, 1961   2:00 P.M.

6. Circulation of the Fluids of the Inner Ear

   Merle Lawrence, Ph.D.

7. Some Vestibular Problems in Space Medicine

   Joseph A. Sullivan, M.B., F.R.C.S.(C), Walter H. Johnson,
   Ph.D., J. Brydon Smith, M.B., F.R.C.S.(C)
   Discussor: Col. Ralph Kraus, U.S.A.F.

8. The Effects of Kanamycin, Asphyxia, and Acoustic Trauma on the
   Permeability of the Cochlear Partitions

   Geo. Misrahy, M.D., Ph.D. (by invitation)
   Discussor: Joseph E. Hawkins, M.D.

9. The Effect of Sensorineural Lesions on Pitch Discrimination in Cats

   Donald Elliott, Ph.D. (by invitation), Harold F. Schuknecht,
   M.D.

10. Histopathologic Findings Following Stapes Surgery in the Human

    John R. Lindsay, M.D.

SATURDAY MORNING, MAY 27, 1961   9:00 A.M.

1. Stapedial, Capsular and Labyrinthine Anatomy in Relation to
   Otologic Surgery

   Barry J. Anson, Ph.D.

2. A Clinical and Laboratory Evaluation of Polyethylene Tubing in
   Middle Ear Surgery

   Francis A. Sooy, M.D.

3. Relation of Identification Audiometry and Otologic Conditions

   Raymond E. Jordan, M.D., Eldon L. Eagles, M.D. (by invitation)

4. The Further Destruction of a Deafened Child's Hearing by the Use of Powerful Hearing Aids

   Chas. E. Kinney, M.D.
   Discussion: S. Richard Silverman, Ph.D.

SATURDAY AFTERNOON, MAY 27, 1961   2:30 P.M.

5. Placebos, Antisludging Drugs and Disorders of the Ears

   Edmund Prince Fowler, M.D.

6. Age, Noise and Hearing Loss

   Aram Glorig, M.D., Hallowell Davis, M.D., Ph.D.

7. Acoustic Measurements of Middle Ear Function

   Joseph Zwislocki, Ph.D. (by invitation)

8. Animal Experiments on the Inner Ear (moving picture)

   Albert Hohman, M.D.

THE AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY

Lake Placid Club, Essex County, New York

SCIENTIFIC PROGRAM

TUESDAY, MAY 23, 1961   9:30 A.M.

Presidential Address

The Responsibility of the Otolaryngologist in the Prevention and Care of Automobile Injuries and Deaths

Fletcher D. Woodward, M.D., Charlottesville, Va.

E.N.T. in Re-ENT-ry

James Milton Robb, M.D., Detroit, Mich. - *Guest of Honor*

1. The Frequency and Severity of Injury to the Face and Jaws Associated with Automobile Accident Injuries

    John O. Moore, Ph.D., Sayville, L.I., N. Y. (by invitation)

2. The Immediate Repair of Injuries of the Face and Jaws

    Edgar M. Holmes, M.D., Boston, Mass.

3. Concepts in Facial Form and Function Rehabilitation

    John J. Conley, M.D., New York, N. Y.

4. Physiology and Pathology of the Cricothyroid Muscle (candidate's thesis)

    Godfrey E. Arnold, M.D., New York, N. Y.

WEDNESDAY, MAY 24, 1961   9:30 A.M.

5. A Laboratory Study on Duration and Effect of IV Estrogen on Small Blood Vessels

    Maurice Schiff, Captain MC USN, H. Burn, M.S. (by invitation), both from U.S. Naval Hosp., Oakland, Cal.

6. Problems of Weightlessness: Otolaryngological Aspects

    Paul A. Campbell, Colonel MC USAF, Brooks Air Force Base, Texas

7. Lymphatics of the Larynx and Neck

    Joel Jay Pressman, M.D., Los Angeles, Calif.

8. Carcinoma of the Epiglottis - Importance of Early Diagnosis and Treatment

    William A. Lell, M.D., Phliadelphia, Pa.

9. Functional Restitution of the Food Passage in Extensive Stenosing Caustic Burns of the Pharynx and Esophagus

Joseph H., Ogura, M.D., Charles L. Roper, M.D. (by
invitation), Thomas H. Burford, M.D. (by invitation),
all of St. Louis, Mo.

THURSDAY, MAY 25, 1961   9:30 A.M.

10. Variations in Normal Hearing: An Anatomical Explanation
Based on Area-1 Ratio

William H. Saunders, M.D., Columbus, Ohio (by invitation)

11. A Five-Year Report on Fenestration of the Oval Window with
Vein Graft   (Illustrated with Color Movie)

John J. Shea, M.D., Memphis, Tenn. (by invitation)

12. Decompression of the Facial Nerve in Experimental Bell's Palsy
in the Dog

Francis H. McGovern, M.D., Danville, Va.; J. S. Hansel,
M.D., Danville, Va. (by invitation)

13. Motion Picture, Surgery of the Facial Nerve

George E. Shambaugh, Jr , M.D., Chicago, Ill.; Eugene L.
Derlacki, M.D., Chicago, Ill.; Hollie E. McHugh, M.D.,
Montreal, Canada; Jesse Waller, M.D., Chicago, Ill., and
Towfik Girgis, M.D., Chicago, Ill. (both by invitation)

AMERICAN MEDICAL ASSOCIATION

Section on Laryngology, Otology and Rhinology

June 1961 Meeting, Coliseum, New York City

TUESDAY, JUNE 27   1:30 P.M.

Unilateral Conduction Loss in the Absence of Middle Ear Inflamma-
tion

James A. Donaldson, M.D., University Hospital, Iowa City, Iowa

Address of Guest of Honor

    Gordon D. Hoople, M.D., Syracuse, New York

Address of Section Chairman

    Lawrence R. Boies, M.D., Minneapolis, Minnesota

Septal Dermoplasty

    William H. Saunders, M.D., Ohio State University, Columbus 10, Ohio

        Discussion to be opened by John Kirchner, M.D., Yale University, New Haven, Connecticut

Experiences with the Trans-Septal Trans-Sphenoidal Route in Hypophysectomy for Metastatic Carcinoma of the Breast

    J. T. Nogeura, M.D., and F. Robert Haase, M.D., both of 601 Grand Avenue, Asbury Park, New Jersey

        Discussion to be opened by David Myers, M.D., Temple University, Philadelphia 40, Pa.

New Concept in Rhinoplastic Procedures

    Lyndon A. Peer, M.D., East Orange, New Jersey

        Discussion to be opened by John Marquis Converse, M.D., New York City

Safe Removal of the Nasal Hump

    Irving B. Goldman, M.D., New York City

        Discussion to be opened by Irvin J. Fine, M.D., Perth Amboy, New Jersey, and John T. Dickson, M.D., Pittsburgh, Pa.

Results of the Treatment of Ménière's Disease with Ultrasonic Waves

    Franz Altmann, M.D., and Jules G. Waltner, M.D., both of New York City

WEDNESDAY, JUNE 28   1:30 P.M.

Bronchoscopy Under General Anesthesia—A Simplified Safe Method

    L. Q. Pang, M.D., 1374 Nuuanu Avenue, Honolulu 17, Hawaii

Discussion to be opened by Lyle Waggoner, M.D., Detroit, Michigan, and DeGraaf Woodman, M.D., New York City

Corrosive Esophagitis

John F. Daly, M.D., New York City, and John C. Cardona, M.D., New York City

Discussion to be opened by F. Johnson Putney, M.D., Philadelphia, Pa., and Daniel C. Baker, M.D., New York City

Conservation of Hearing: A Clinical Analysis of Current Concepts

J. M. Cole, M.D., Danville, Pennsylvania

Clinical Application of Newer Hearing Tests

Fred Harbert, M.D., Philadelphia, Pennsylvania

Discussion to be opened by E. P. Fowler, Jr., M.D., New York City, and Moe Bergman, M.D., Hunter College, 695 Park Ave., N. Y. 21, N. Y. (probably by invitation)

Secretory Otitis Media—Problems and Pitfalls

B. W. Armstrong, M.D., Charlotte, North Carolina

Discussion to be opened by Frank Lathrop, M.D., Boston, Mass., and Francis Davison, M.D., Danville, Pennsylvania

Tympanoplasty—Its Trends

Woodrow D. Schlosser, M.D., 3701 N. Broad St., Philadelphia, Pa.

Discussion to be opened by Lindsay L. Pratt, M.D., Philadelphia, Pa., and Louis Silcox, M.D., Philadelphia, Pa.

The Surgical Technique of Fenestration of the Oval Window (with new film)

John J. Shea, M.D., Memphis 5, Tennessee

Vascular Surgery in Operation on the Head and Neck

John M. Loré, Jr., M.D., Hemion Road, Suffern, New York

Discussion to be opened by John L. Madden, M.D., St.
Clare's Hospital, New York City, and Ralph J.
Greenberg, M.D., Good Samaritan Hospital,
Suffern, New York

THURSDAY, JUNE 29

Instruction Courses in Surgery of the Ear, Nose and Throat

Admission by ticket, available on the two preceding days

UNIVERSITY OF PENNSYLVANIA

The University of Pennsylvania Graduate School of Medicine announces full-time courses in Otolaryngology, Bronchoesophagology and Laryngeal Surgery.

Courses in otolaryngology and bronchoesophagology are now divided into two semesters of four months each. During the first semester (October to January), emphasis is placed upon basic medical sciences. Cadaver endaural surgery of the temporal bone, rhinoplasty, laryngeal surgery and bronchoesophagology are given in the second semester (February to May).

These courses are recognized for credit toward qualification by the American Board of Otolaryngology.

Registration will be limited to fifteen physicians.

Graduate School of Medicine
36th and Hamilton Walk
Philadelphia 4, Pa.

UNIVERSITY OF TORONTO

On May 11, 12 and 13, 1961, there will be presented a graduate course by the Staff of the Department of Otolaryngology. They will be assisted by two distinguished guests: Dr. Philip E. Meltzer, Profes-

sor of Otolaryngology, Harvard Medical School, Chief of Otolaryngology, Massachusetts Eye and Ear Infirmary; and Dr. W. G. Hemenway, Department of Otolaryngology, University of Chicago.

The first session will begin in the afternoon of May 11th, in the Royal York Hotel, Toronto, in association with the Section of Otolaryngology of the Ontario Medical Association. The remainder of the sessions will be held in the Clinical areas of the University of Toronto.

The fee for the course will be $40.00 and will include a complimentary dinner.

Please address all inquiries to the Director, Division of Postgraduate Medical Education, University of Toronto.

TEMPLE UNIVERSITY

Temple University School of Medicine announces the following courses to be given during the next year:

Postgraduate course in Bronchoesophagology, September 11 to 22, 1961, and January 15 to 26, 1962. Postgraduate course in Laryngology and Laryngeal Surgery, April 2 to 13, 1962.

These courses are to be given in the Department of Laryngology and Bronchoesophagology, Temple University Medical Center, under the direction of Drs. Charles M. Norris and Walter H. Maloney.

The tuition fee for each course is $250. Application and further information may be obtained by writing to: Chevalier Jackson Clinic, Temple University Medical Center, 3401 N. Broad Street, Philadelphia 40, Pa.

ROYAL SOCIETY OF MEDICINE, LONDON

Programs for the 1961 sessions of the Section of Laryngology will be on the following subjects:

March 3—Chronic sinusitis in children.

May 5—Vasomotor rhinitis.

Those of the Section of Otology will be:

March 3—1. The pathological bases of some labyrinthine vascular disorders. 2. Meniere's syndrome.

May 5—The present position of stapes footplate surgery.

Members of the American Laryngological Association, the American Otological Society and the American Triological Society who will be in the United Kingdom at the time of any of these meetngs will be very welcome.

CASSELBERRY PRIZE

A sufficient fund having accrued from the Casselberry Fund for encouraging advancement in the art and science of Laryngology and Rhinology, this sum is now available in part or as a whole, for a prize award. Theses must be in the hands of the Secretary of the American Laryngological Association prior to December 1 of any given year.

The Award is a prize of money with accompanying certificate signed by the officers of the American Laryngological Association. The sum of money will be agreed upon by the Council of the Association after the manuscript has been evaluated by the Award Committee. It may be awarded in whole or in part among several contestants.

Eligible contestants may be: 1. Hospital interns, residents, or graduate students in rhinology and laryngology; 2. An individual with an M.D. degree who is actively practicing or teaching rhinology and laryngology in the Americas; 3. Any scientific worker in the field of rhinology and laryngology.

Manuscripts shall be presented to the Secretary of the Association under nom de plume which shall in *no way* indicate the author's identity. There shall also be a sealed envelope bearing the nom de plume and containing a card showing the name and address of the contestant which the Secretary shall keep in his possession.

Manuscripts must be limited to 5000 words and must be type-written in double spacing on one side of the sheet. The thesis shall not have been published elsewhere before submission.

The successful thesis shall become the property of the American Laryngological Association but this provision shall in no way interfere with publication of the thesis in the Journal of the author's choice.

The Award which will be made at the Annual Meeting of the American Laryngological Association shall be based on:

1. Originality of materal

2. Scientific and clinical value

3. Suitability for this Award

4. Method of presentation as to style, illustrations and reference

The maximum amount of the Award shall not exceed $200.00.

ACADEMY AWARDS

Each year the American Academy of Ophthalmology and Otolaryngology offers awards for outstanding investigative work performed during residency training. These awards are an expression of the high value which the American Academy of Ophthalmology and Otolaryngology places on original effort as the basis of medical progress.

The main purpose of the awards is to give recognition for outstanding investigations performed by young physicians who have focused their attention on otolaryngology. The Academy also hopes that the award program will provide an extra stimulus for those who have investigative ideas as well as a stimulus to department heads to provide time and facilities so that their students pursue these ideas.

Separate awards will be given for clinical and for basic investigations in the broad field of otolaryngology. The broad field of otolaryngology includes the ear, nose, throat, nasopharynx, oral cavity, larynx, esophagus, tracheobronchial tree and neck. Clinical investiga-

tion is understood to mean any study involving human patients which contributes information regarding the symptomatology, etiology, diagnosis, course, complications, therapy, etc., of any otolaryngological disorder. Basic investigation includes any study which involves histolgoic, physiologic, audiolgoic, experimental-surgical and other similar procedures or lines of investigation. Research may be both of the clinical and basic types, such as a study involving both humans and animals, and the Awards Committee will decide in which category such a manuscript is to be considered.

The competition is open to Doctors of Medicine who have completed at least one year of internship (not necessarily in the United States or Canada) and who began resident training in otolaryngology no longer than five years past. Residency training must be in an approved American or Canadian hospital but the contestant need not be an American or Canadian citizen. The investigative work must have begun during the normal three or four year residency program but may be completed afterward. The majority of the investigative work must have been performed by the contestant, although he may acquire needed advice and technical assistance. The work need not be entirely original and may represent a continuation of research already in progress in a laboratory. The author's name should appear on the title page. Co-authors may be listed, but the contestant must be the first author. When an equal contribution to the investigation has been made by two or more qualified contestants, a letter should accompany the manuscript stating this fact. A cash award made for an entry having two or more qualified authors will be divided equally between these authors.

The Academy wishes to allow the contestant complete freedom in the publication of the manuscript. Thus, both published and unpublished papers will receive equal attention so long as they are submitted within the time limitations indicated. Reprints will be accepted, if submitted within one year of publication. Manuscripts must be typewritten and follow accepted style for journal publication. An accompanying letter should state whether the manuscript has been published or has been submitted for publication.

Judgments of merit will be based on scientific content as well as the manner of presentation. Manuscripts should contain a minimum of historical detail, review of the literature and statements of opinion.

The manuscripts must be in the hands of Dr. Juergen Tonndorf, University Hospitals, Iowa City, Iowa, by the 31st of December, 1961.

Awards will be made at the discretion of the Committee on Research and Finance of the Council of the American Academy of Ophthalmology and Otolaryngology and may be withheld if there are no manuscripts of merit.   Cash awards shall not exceed six in number and shall not total more than $5000.00 in any one year.   The award may be made for either clinical or basic research.   Certificates of Merit may be awarded for exceptional manuscripts not winning cash awards.   Letters in support of manuscripts will not be accepted by the Awards Subcommittee.

G. O. Proud, M.D., Chairman, Council

Committee for Research in Otolaryngology

American Academy of Ophthalmology and Otolaryngology

AMERICAN ACADEMY

The 1961-1962 Home Study Courses in the basic sciences related to ophthalmology and otolaryngology, which are offered as a part of the educational program of the American Academy of Ophthalmology and Otolaryngology, will begin on September 1 and continue for a period of ten months.   Detailed infromation and application forms can be secured from Dr. William L. Benedict, the executive secretary-treasurer of the Academy, 15 Second Street S.W., Rochester, Minnesota.   Registrations should be completed before August 15.

UNIVERSITY OF BORDEAUX

A graduate course in Functional Otological Microsurgery will be conducted by Associate Professor Michel Portmann, M.D., July 3-13, 1961.   The course will be given in English and will be limited to twenty doctors of medicine who are certified otolaryngologists.   The fee will be $150.00 in advance.   For further information please address Dr. Michel Portmann, 45 Cours Maréchal Foch, Bordeaux, France.

AMERICAN BOARD OF OTOLARYNGOLOGY

The American Board of Otolaryngology will conduct only one examination in 1961, and this will be October 2-5, 1961, in Chicago, Illinois, at the Palmer House.

Dean M. Lierle, M.D., Secy.

ANNALS

In order to fulfill the requests for the March 1935, March 1937, March 1955, March 1956, December 1958, March 1959 and June 1959 issues, the ANNALS will pay $3.50 for each book in good condition.

Please mail books to Zimmerman-Petty Linotyping Co., 2636 Locust St., St. Louis 3, Mo.

OFFICERS

AMERICAN OTOLOGICAL SOCIETY

President: Henry L. Williams, M.D., Rochester, Minn.

Secretary-Treasurer: James A. Moore, M.D., New York Hospital, 526 E. 68th St., New York 21, N. Y.

Meeting: Lake Placid, N.Y., May 26-27, 1961

VII INTERNATIONAL CONGRESS OF OTOLARYNGOLOGY

President: Prof. M. Aubry, Paris

Sec. Gen.: Dr. H. Guillon, 6 Ave. Mac-Mahon, Paris XVII France

Meeting: Paris, July 15-22, 1961

INTERNATIONAL BRONCHOESOPHAGOLOGICAL SOCIETY

President: Dr. Jo Ono, Tokyo

Secretary: Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40, Pa.

PAN-AMERICAN ASSOCIATION OF OTO-RHINO-LARYNGOLOGY AND BRONCHO-ESOPHAGOLOGY

President: Dr. Jose Gros, Havana

Secretary: Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40, Pa.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: John F. Tolan, M.D., 1118 - 9th Avenue, Seattle 1, Wash.

Secretary-Treasurer: Homer E. Smith, M.D., 508 East South Temple, Salt Lake City, Utah

CANADIAN OTOLARYNGOLOGICAL SOCIETY

President: Dr. Fernand Montreuil

Secretary: Dr. Donald M. MacRae, 324 Spring Garden Road, Halifax, Nova Scotia

MEXICAN SOCIETY OF OTOLARYNGOLOGY

President: Dr. Rafael Giorgana

Secretary: Dr. Carlos Valenzuela, Monterrey 47 Mexico 7, D.F.